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Allergic Shock to Latex and Ethylene Oxide During Surgery for Spina Bifida

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There is increasing awareness of anaphylaxis to latex during surgery.[1–5] Although children with spina bifida are not known to be specifically atopic or to be predisposed to developing drug allergies, we present three cases that lead us to discuss this hypothesis.

REPORT OF THREE CASES

Case 1

A 13-yr-old girl with spina bifida and a thoracolumbar meningocele presented in March 1989 with severe anaphylactic shock and bronchospasm during a tenth surgical procedure. These started 90 min after she had been given ketamine, flunitrazepam, and atropine, 75 min after phenoperidine and vecuronium, and 15 min after the start of the surgical procedure itself. Epinephrine 0.75 mg and crystalloid were administrated intravenously. Anesthesia was maintained with nitrous oxide and isoflurane. She had had bronchial asthma since early childhood, as well as several adverse reactions to nonsteroidal antiinflammatory drugs and contrast media with iodine. She had, at one time, developed facial and thoracic edema after having sucked on a plastic syringe. During the immunologic outpatient visit, she developed a rash on her right hand after touching the tubing of an aerosol apparatus, a reaction suggestive of immediate hypersensitivity.

Investigations carried out in June 1989 revealed a hypersensitivity to airborne allergens, confirmed by skin tests to the principal mites. IgE concentration was 381 kilo international units (KIU) $\cdot l^{-1}$ (normal < 120 KIU $\cdot l^{-1}$). Bronchial hyperreactivity was demonstrated with the carbachol test.

Intradermal tests carried out with the different muscle relaxants were negative. The radioimmunoassay (RIA) with quaternary ammonium showing specific IgE to muscle relaxants was negative. Human basophil degranulation tests with penicillin, netilmicin, and atracurium were also negative.

An allergy to latex was demonstrated with skin prick tests (epidermal puncture) performed through a drop of latex emulsion (colloidal suspension with prevulcanized natural rubber particles), and through two surgical gloves. The prick test was much more positive for the glove sterilized with ethylene oxide (EO) than for the glove sterilized with gamma rays. A radioallergosorbent test (RAST) revealed a low concentration of specific anti-latex IgE (0.65 PRU $\cdot$ ml^{-1}). This concentration may have been artificially low because anaphylaxis had occurred relatively recently. The RAST with EO was very strongly positive, with an isotope count 20 times that of control (a disk of human serum albumin). This confirmed the diagnosis of an allergy to latex and to EO.

One month after these tests, a further operation was carried out with no complications, with the following preventive measures: careful rinsing of intravenous infusion kits, avoidance of all latex, and avoidance of all equipment disinfected with EO.

Case 2

A 14-yr-old boy required his 24th surgical procedure in October 1987. This child had spina bifida with a myelomeningocele and had a past history of asthma. Anaphylaxis occurred 40 min after the start of surgery. At that time, the anesthetist noticed generalized wheezing with increased airway pressure. The concentration of halothane was increased, and salbutamol was administered, but without relief of symptoms; further doses of vecuronium and alfentanil were given. Systolic blood pressure decreased from 100 to 40 mmHg, with a concomitant tachycardia of 160 bpm and peripheral cyanosis. After treatment with 0.25 mg iv epinephrine, and an increase in blood pressure, a generalized rash appeared. The epinephrine infusion was maintained for 24 h.

Investigations carried out twice (6 and 18 months after this incident) did not show any evidence of anaphylaxis to alfentanil or vecuronium. The incident was believed, at that time, to be due to nonspecific histamine release due to the anesthetic drugs.

Further tests carried out in June 1989 showed a total IgE concentration of 135 KUI $\cdot l^{-1}$, negative skin tests to common airborne allergens, a negative Phadiatop test (Pharmacia, France; a RIA that rules out any specific IgE to common inhalants[6]). All of the tests with muscle relaxants, alfentanil, and thiopental remained negative. The epidermal puncture through a drop of latex emulsion was very strongly positive. Pricks carried out through gloves sterilized with gamma rays or EO gave a more definite reaction with the latter. The RAST was positive with latex, at 1.46 PRU $\cdot$ ml^{-1}, but negative with EO. Therefore, the final diagnosis was true anaphylactic shock due to latex, with a possibility of an associated allergy to EO.

Case 3

A 9-yr-old girl with a myelomeningocele had undergone ten previous procedures, all uneventful. She had required bladder catheterization four times per day, using latex catheters sterilized with EO. During the latest surgical procedure (an enlargement enterocystoplasty for neurologic bladder), she had tachycardia, a decrease in blood pressure, and a generalized erythematous rash which began approximately 1 h after the start of anesthesia (flunitrazepam, thiopental, phenoperidine, vecuronium, and isoflurane). This incident was successfully treated with dexamethasone and dobutamine.

All tests for anesthetic drugs were negative. The child was not atopic. Prick tests with latex were positive, as were tests carried out through a latex glove sterilized with EO. The prick test carried out through a latex glove sterilized with gamma rays was only weakly positive. RASTs with latex and EO were positive.

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Discussion

Circumstances in which there may be an allergy to latex include the wearing of gloves,[7-12] repeated oral contact with toy balloons,[1-3§] rubber dams, dental casts, urinary or intestinal catheters,[3-4] surgical gloves during gynecological examinations,[13] or surgical procedures.[1-3-4-5] Sensitization to latex seems frequent in medical and surgical personnel: Turjanmaa has reported an incidence of latent sensitization to latex of 6.4%.[14] It has also been shown that atopic subjects are more likely to develop an allergy to latex; 75% of patients allergic to latex were atopic.[4-14]

Latex allergens are water soluble proteins contained in the natural gum used to make gloves, and remain in the finished product. They are resistant to the high temperatures used for vulcanizing (100° C for 5 min) and to the chemical agents used to speed up vulcanization. Molecular weights range from 2,000 to 30,000 d. The finished product is an isoprene polymer that contains 2 to 3% protein. Latex specific IgE are easily demonstrated by skin prick tests, leukocyte histamine release, human basophil degranulation, immunoenzymatic assays, or RIAs.[11,15-19]

EO has been shown to be responsible for anaphylactic shock in hemodialysis centers.[20-21] Specific antibodies were identified by Dolovitch and Bell[22]; they later were found in 9% to more than 40% of hemodialysis patients, who did not necessarily have corresponding clinical reactions.[20-23] EO sensitization occurs also during plateletpheresis.[24] We reported a case of generalized reaction to the wearing of gloves sterilized with EO in an auxiliary nurse. One year later, she had a severe anaphylaxis when she had urinary catheterization in the obstetrics department.[2]

EO acts as an alkylating agent for sulfhydryl, carboxyl, hydroxyl, and amino radicals. It therefore can react with a great variety of proteins, and so is a complete, powerful antigen. The sensitization is possible after only a few contacts with plastic bags used for cytapheresis sterilized with EO; these give, at most, 1 μg EO per milliliter effluent.

Slater[25] reported two cases of patients with spina bifida, who presented during surgery with shock related to a latex allergy. As far we can ascertain, the cases reported here are the first to show a double IgE-dependent sensitization to both a hapten (EO) and a protein allergen (latex). The diagnostic was confirmed by positive RAST to both substances in case 1. Comparing prick tests carried out through gloves sterilized with gamma rays or EO is very significant. In our three cases, prick tests through gloves sterilized with EO were much more positive than were those through gloves sterilized with gamma rays; it seems that, by this means, sensitization is demonstrated not only to latex but also to EO.

Children with spina bifida may be at risk of anaphylaxis to both substances. The frequent contact with surgical gloves, due to the great number of surgical procedures, is an obvious sensitization factor. To this must be added daily contacts with urinary catheters (made with latex and sterilized with EO) as well as with intravenous infusion tubing, also sterilized with EO. However, we should consider the possibility of a genetic predisposition to developing atopy or drug allergies in children with spina bifida. One of Slater's[25] cases had a past history of asthma and an allergy to phenytoin. Two of the cases reported here had a past history of asthma; one was atopic and had had different adverse drug reactions. This hypothesis is now under study.[26]

In light of these cases, we recommend the avoidance of all latex urinary catheters and other equipment sterilized with EO for children with spina bifida, in whom multiple surgical procedures or daily catheterization are necessary. For patient care, plastic catheters and equipment sterilized with gamma rays, single-use gloves in polyvinyl chloride, or polyethylene can be used. The gloves used during surgical procedures should be only those sterilized with gamma rays. It is not very realistic to suggest replacing, for all patients, latex gloves with neoprene (synthetic rubber) gloves: neoprene gloves are thicker, and many surgeons prefer not to use them. Since prick tests and RASTs are reliable for detecting latex allergy and are easy to perform, we suggest performing them routinely in children with spina bifida, before each new surgical procedure, to permit detection of sensitization. Because of the great differences in allergenic character between gloves with different trademarks, it seems highly likely that "hypoallergenic" gloves could be made available in the future; some trademarked gloves are, in fact, already hypoallergenic.[27]

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References

1. Axelsson JGK, Johansson SGO, Wrangsjö K: IgE-mediated anaphylactoid reactions to rubber. Allergy 42:46–50, 1987
2. Olivieri P, Berchet-Montaut MP, Thomas P: Analgésie obstétricale chez une femme allergique à l'oxyde d'éthylène. Ann Fr Anesth Réanim 7:346–348, 1988
3. Gerber AC, Jorg W, Zbinden S, Seger RA, Dangell PH: Severe intraoperative anaphylaxis to surgical gloves: Latex allergy, an unfamiliar condition. ANESTHESIOLOGY 71:800–802, 1989
4. Fabro L, Muhlethaler K, Wuthrich B: Anaphylaktische Reaktion auf Latex, ein Soforttypallergen von Zunehmender Bedeutung. Hautarzt 40:208–211, 1989
5. Leynadier F, Pecquet C, Dry J: Anaphylaxis to latex during surgery. Anaesthesia 44:547–550, 1989
6. Merrett J, Merrett TG: Phadiatop-A novel IgE antibody screening test. Clin Allergy 17:409–416, 1987
7. Nutter AF: Contact urticaria to rubber. Br J Dermatol 101:597–598, 1979

8. Forstrom L: Contact urticaria from latex surgical gloves. Contact Dermatitis 6:33–35, 1980
9. Medin B, Fregert S: Contact urticaria from natural latex gloves. Contact Dermatitis 6:52–53, 1980
10. Estlander T, Jolanki R, Kanerva L: Dermatitis and urticaria from rubber and plastic gloves. Contact Dermatitis 14:20–25, 1986
11. Carrillo T, Cuevas M, Munoz T, Hinojosa M, Moneo I: Contact urticaria and rhinitis from latex surgical gloves. Contact Dermatitis 15:69–72, 1986
12. Spaner D, Dolovich J, Tarlo S, Sussman G, Butoo K: Hypersensitivity to natural latex. J Allergy Clin Immunol 83:1135–1137, 1989
13. Turjanmaa K, Reunala T, Tuimala R, Karkkainen T: Allergy to latex gloves: Unusual complication during delivery. Br Med J 297:1029, 1988
14. Turjanmaa K: Incidence of immediate allergy to latex gloves in hospital personnel. Contact Dermatitis 17:270–275, 1987
15. Frosch PJ, Wahl R, Bammer FA, Maasch HJ: Contact urticaria to rubber gloves in IgE-mediated. Contact Dermatitis 14:241–245, 1986
16. Wrangsjö K, Mellström G, Axelsson G: Discomfort from rubber gloves indicating contact urticaria. Contact Dermatitis 15:79–84, 1986
17. Wrangsjö K, Wahlberg JE, Axelsson IGK: IgE-mediated allergy to natural latex in 30 patients with contact urticaria. Contact Dermatitis 19:264–271, 1988
18. Turjanmaa K, Räsänen L, Lehto M, Mäkinen-Kiljunen S, Reunala T: Basophil histamine release and lymphocyte proliferation tests in latex contact urticaria. Allergy 44:181–186, 1989
19. Turjanmaa K, Reunala T, Räsänen L: Comparison of diagnostic methods in latex surgical glove contact urticaria. Contact Dermatitis 19:241–247, 1988
20. Bommer J, Barth HP, Wilhelms OH, Schindele H: Anaphylactoid reactions in dialysis patients: Role of ethylene-oxide. Lancet 1382–1384, 1985
21. Kessler M, Cao Huu T, Mariot A, Chanliau J: Hemodialysis-associated complications due to sterilizing agents ethylene oxide and formaldehyde. Contrib Nephrol 62:13–23, 1988
22. Dolovich J, Bell B: Allergy to a product of ethylene oxide gas: Demonstration of IgE and IgG antibodies and hapten specificity. J Allergy Clin Immunol 62:30–32, 1978
23. Marshall CP, Sagona MA, Wathen RL, Ward RA, Dolovich J: Reactions during hemodialysis caused by allergy to ethylene oxide gas sterilization. J Allergy Clin Immunol 5:653–657, 1988
24. Leitman SF, Boltansky H, Alter HJ, Pearson FC: Allergic reactions in healthy plateletpheresis donors caused by sensitization to ethylene oxide gas. N Engl J Med 315:1192–1196, 1986
25. Slater JE: Rubber anaphylaxis. N Engl J Med 320:1126–1130, 1989
26. Moneret-Vautrin DA, Mata E, Guéant JL, Turgeman D, Laxenaire MC: High risk of anaphylactic shock during surgery for spina bifida. Lancet 335:865–866, 1990
27. Turjanmaa K, Laurila K, Mäkinen-Kiljunen S, Reunala T: Rubber contact urticaria: Allergenic properties of 19 brands of latex gloves. Contact Dermatitis 19:362–367, 1988

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Segmental Manifestation of Reflex Sympathetic Dystrophy Syndrome Limited to One Finger

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The reflex sympathetic dystrophy syndrome (RSDS) consists of multiple symptoms, including vasomotor instability, swelling, and chronic pain involving the affected extremity.[1,2] It is a dynamic process and may progress insidiously through three stages over several months.

The clinical features of stage 1 in the upper extremity are swelling, pain, and moderate stiffness of the joints in the fingers and wrist. The burning pain may be precipitated or exacerbated by exposure to cold. The skin may be pale or red and is usually moist because of hyperhydrosis.

Stage 2 is characterized by persistent burning pain in the hand associated with marked stiffness of the wrist and fingers. Atrophy of the muscles produces weakness of the hand, and eventually, flexion deformities of the fingers. The skin usually is pale, cold, and dry.

These symptoms may subside, and the dystrophic changes frequently may be reversed with therapy. Some patients may recover spontaneously. About 20% of stage-2 patients will succumb to stage 3.[3] These patients demonstrate irreversible muscle wasting, contractures, and osteoporosis progressing to Sudeck's atrophy, eventuating in total and permanent loss of function.

The RSDS may be precipitated by catastrophic events such as cardiac surgery,[3] myocardial infarction,[4] cerebrovascular accident,[5] or spinal cord injury.[6] Conversely, it may be triggered as an exaggerated response to any minimal trauma of the hand. Examples include finger fracture, wrist sprain, and minor hand surgery, such as a nail biopsy.[7] About 3% of surgical procedures of the hand and arm may demonstrate symptoms characteristic of RSDS.[3]

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