

Perioperative collapse: prevalence of latex allergy in patients sensitive to anaesthetic agents

B. B. TAN¹, J. T. LEAR¹, J. WATTS², P. JONES³ AND J. S. C. ENGLISH¹

Departments of ¹Dermatology and ²Anaesthetics, North Staffordshire Hospital

³Department of Mathematics, Keele University, Keele, UK

The evidence in the literature suggests that the prevalence of latex allergy in the general population is approximately 1%. With increasing awareness of transmission of HIV and other infections such as hepatitis B, the use of latex gloves and condoms has escalated in recent years. As cheaper latex gloves of variable and doubtful quality flood the market, health care workers and patients are being increasingly sensitized by these latex products. A retrospective study investigated the prevalence of latex allergy in a cohort of 26 patients who suffered perioperative anaphylactoid reactions. 84% of these patients were hypersensitive to at least 1 anaesthetic-related agent. 7.7% were also allergic to latex ($p=0.028$). Atopy is a strong predisposing factor ($p=0.006$). An accurate preoperative history of atopy and past reactions to latex will identify most at-risk patients. Prick test and RAST to latex will confirm the latex allergy. Anaesthetists, surgeons, allergists and other health practitioners should be aware of this problem.

Key words: perioperative anaphylactoid reactions; hypersensitivity to anaesthetic-related agents; latex allergy; atopy; non-latex products; allergen replacement; prevention. © Munksgaard, 1997.

Accepted for publication 5 November 1996

Although contact dermatitis due to delayed hypersensitivity reactions to latex and rubber has been recognized for 40 years, the first Type I reaction was reported only 18 years ago (1). With increasing awareness of the transmission of HIV and other infections such as hepatitis B, the use of latex gloves among health care workers has much increased. The Occupational Safety and Health Administration estimated that more than 5.6 million American health care and other workers use latex gloves regularly: over 7 billion pairs of gloves a year (2). The use of condoms has been encouraged by doctors and the media alike to reduce the risk of HIV infection and other sexually transmitted diseases.

The latex from the rubber tree (*Hevea brasiliensis*) contains many proteins and allergens which cannot be completely removed during the manufacturing process. It has been suggested that the recent increased demand for latex gloves and other products such as condoms has resulted in the manufacturing of less-refined products containing higher concentrations of latex allergens (3). There is also considerable variation in the total protein and allergen contents of the different latex glove brands (4).

There are an increasing number of reports of serious and unexpected reactions to devices containing natural latex, associated with surgery (4-7), barium enema (8), vaccination (9) and even a game of squash (10). The evidence in the literature suggests that the prevalence of latex allergy in the general population is approximately 1% (11). In contrast, it is estimated that 3%-21% of health care workers, especially those who wear rubber gloves frequently, e.g., surgeons, anaesthetists, nurses and dentists are hypersensitive to latex (12-21). 1 study found that as many as 53% of laboratory technicians had reactions to latex gloves (22). A significant number of patients with spina bifida and/or urological abnormality who develop intraoperative anaphylaxis are allergic to latex (23-28). The prevalence of atopy in this group of patients is higher than the accepted 2-20% in the normal population (25, 29, 30). Frequent past exposure leading to sensitization is also a predisposing factor (27).

Anaphylactic reactions to anaesthetic and associated agents are well-recognized and both intradermal (i.d.) and prick testing are used to diagnose the drugs responsible for acute reactions (31-33). There have been only 2 reports of patients who

developed intraoperative collapse due to allergy to a combination of a muscle relaxant and latex (34, 35).

In this study, we investigated the prevalence of latex allergy in a cohort of patients who developed intraoperative anaphylaxis.

Materials and Methods

Hospital ethical committee approval was obtained. Between 1979–1994, 37 patients developed perioperative anaphylactoid reactions in the North Staffordshire Hospital; these patients represent virtually all perioperative anaphylactoid reactions during this period. The diagnosis of an anaphylactoid reaction was based on 1 or more of the following clinical features: cardiovascular collapse, bronchospasm, oedema and rash. I.d. tests were performed 6 weeks later with relevant anaesthetic agents and muscle relaxants in all patients. The drugs chosen were intravenous agents to which the patient was exposed before the anaphylactoid reaction and included hypnotics, analgesics and anti-cholinergics. 0.2 ml of 1:1000 dilutions of drugs not known to release histamine and 1:10 000 dilutions of drugs known to release histamine (e.g., d-tubocurarine and opioids) were injected into the volar aspect of the forearm. A negative control using normal saline was included in each patient. The criterion for a positive response was a wheal and flare of >1.5 cm diameter at those dilutions at 30 min.

Retrospectively, these patients were recalled and invited to undergo prick tests (PT) with raw latex preserved solely with ammonia (0.7% w/w), especially produced by the Rubber Research Institute of Malaysia, commercial refined latex extracts (natural and gloves), and common aeroallergens (cat, dog, house dust mite, grass and tree) on the volar aspect of the forearm with a sterile lancet. A positive control (histamine) and a negative control (diluent) were included. All commercial PT solutions were supplied by Diagenics, Newark, UK. The test was considered positive if there was a wheal and flare 2 mm larger than diluent control at 15 min. Serum latex-specific IgE antibodies using RAST CAP were measured using a commercially available kit (Kabi Pharmacia Diagnostics, Sweden). A positive prick test to common aeroallergens and a past history of asthma, eczema or hay fever confirmed atopic state (36). A history of past exposure and reactions to latex, and atopic state, was obtained from each patient.

Statistical method

The binomial test was used to obtain the probability of the number of patients observed with

latex allergy and with atopy, assuming they are from a normal population where the prevalence is 1% for latex allergy and 20% in the worst case for atopy.

Results

26 patients ($n=26$; 9 male and 17 female) were available for testing; 3 patients had died, 6 patients had moved away and 2 were unwilling to participate. The mean age of patients when the reaction occurred was 44.3 years (range 15–73 years). 13 out of 26 (50%) had at least 1 positive PT response to aeroallergens and a positive history of asthma, eczema or hay fever confirming atopy. Assuming a prevalence of 20% in the normal population, the probability of 13 or more patients being observed with atopy is 0.006. 21 out of 26 (80.7%) patients developed hypotension, tachycardia and cyanosis consistent with the diagnosis of anaphylaxis. The remaining patients had erythema, wheeze and cough.

22 out of 26 (84.6%) patients gave positive reactions to the 'anaesthetic' agents tested; 5 to suxamethonium (Scoline®), 2 to atracurium (Tracium®), 1 to gallamine (Flaxedil®), 1 to d-tubocurarine (Tubarine®), 1 to pancuronium (Pavulon®), 1 to pentazocine, 3 to papaveretum (Omipon®), 3 to morphine sulphate, 1 to pentothal, 1 to droperidol (Droleptan®), 1 to thiopentone (Intraval®), 5 to alcuronium (Alloferin®), 1 to propofol (Eponal®) and 2 to alphadolone (Althesin®). The latter 3 drugs have been withdrawn from the market. 6 out of 26 (23%) patients were allergic to more than 1 agent. 5 out of 26 (19.2%) patients gave equivocal or negative skin tests.

24 ($n=24$) underwent prick testing with latex (1 patient was pregnant, 1 refused). 5/24 of patients had a positive PT to either raw ammoniated latex and/or refined latex glove extract. 4 out of the 5 patients gave a positive RAST to latex: 1 grade 4 (very high), 1 grade 3 (high) and 2 grade 1 (low).

The patients with grade 3 and 4 reactions were atopic and gave a very good history of acute reactions following contact with certain latex products, e.g., urticaria after vaginal examination, and wearing household gloves. Both patients developed anaphylactic symptoms 20–30 min into surgery. The 1st patient was undergoing an emergency caesarean section and the 2nd patient a total abdominal hysterectomy.

The 2 patients who had grade 1 RAST reactions gave PT responses measuring 2.5 mm and 5 mm greater than the negative control. Neither patient gave a history of hypersensitivity to latex and the weak RAST reactions were considered irrelevant. The 5th patient had a positive PT to latex (5 mm

greater than the negative control) but his RAST to latex was negative. He was atopic and gave positive reactions to all aeroallergens tested, in particular, he had a very strong reaction to grass pollen on prick testing (10 mm greater than the negative control). He did not give a history of allergy to latex and it is possible that, although he was not tested specifically to foodstuffs, the PT reaction to latex represented a cross-reaction with certain foods.

Under very strict criteria for the diagnosis of latex allergy, that is, having positive RAST, PT and history of allergy to latex, we found a total of 2/26 (7.7%) patients, both females, that were considered clinically significant. Assuming a prevalence of 1%, the probability of at least 2 in 26 normal patients being observed with latex allergy is 0.028. This was statistically significant.

If the other 2 patients with positive PT and RAST to latex but with an absent history of latex allergy were also included, the total % of our group of patients considered to be latex-allergic would go up to nearly 15%, making it more statistically significant.

Discussion

The evidence in the literature suggests that about 1% of the general population are allergic to latex (11). An increased prevalence is seen in certain groups, including health care workers, laboratory technicians and patients with spina bifida and urological defects. These groups are more frequently exposed to latex than the general population. Patients undergoing surgery are exposed to latex products and it has been a concern that latex allergy is an underlying cause of intraoperative anaphylaxis. This study was designed to estimate the prevalence of latex allergy in this group of patients. Over 15 years, only 37 patients were referred for investigation of perioperative reactions. Accepting that we have relatively small numbers, we found that 7.7% of our patients were allergic to latex. This was statistically significant. They were also allergic to other drugs (opioids, penicillin, clarithromycin and tetanus toxoid). It would appear that this group of patients suffer from multiple allergies.

Of the 2 patients with grade 1 reactions, 1 had worked in the rubber industry for many years and the 2nd utilized latex products for his leisure activities. As neither patient gave a history of hypersensitivity to latex, we felt that the RAST was irrelevant. Chronic exposure to latex products over many years may have led to very low grade sensitization. It is difficult to speculate as to whether this group of currently asymptomatic patients who have positive tests to latex will develop symptoms

of latex allergy with time, especially if they continue to be exposed to the potential allergen. It may be necessary to repeat PT with latex and to follow up this group of patients for development of symptoms. Some workers suggest that they should be treated as being latex-allergic and advised accordingly.

Pepys, et al. (37) showed that a definite or probable cause was found in 36 of 46 (78.3%) patients who suffered anaesthetic-related anaphylaxis. In this series, suxamethonium was the most frequent culprit and latex was the cause in 2 patients. Our results concur with this, in that 80.7% of our patients gave positive reactions to agents tested, suxamethonium being the commonest drug to react.

We agree with other studies that found atopy to be a predisposing factor in these patients (13, 25, 29). We have shown that latex allergy is a small but significant cause of intraoperative anaphylaxis. At risk-patients can easily be identified preoperatively. Enquiries regarding history of atopy and any reactions to latex should form part of all preoperative assessments. Theatre staff should be informed that non-latex products such as synthetic gloves should be used during surgery.

Acknowledgements

We thank Dr C. G. Male for identifying the study group and for his helpful comments on the manuscript. We are grateful to Dr S. M. Wilkinson and the Rubber Research Institute of Malaysia for their gift of the raw ammoniated latex used for prick testing.

References

1. Nutter A F. Contact urticaria to rubber. *Br J Dermatol* 1979; 101: 597-598.
2. Voelker R. OSHA mandates universal precautions. *AMA news* 16 December 1992.
3. Buccino L A. Latex sensitivity on increase (Experts blame inferior rubber, exposure frequency). *Advance for Medical Laboratory Professionals* 1993: 6-7.
4. Alenius H, Makinen-Kiljunen S, Turjanmaa K, Palosuo T, Reulana T. Allergen and protein content of latex gloves. *Ann Allergy* 1994; 73: 315-20.
5. Dias M, Conchon I, Cortes M, Pereira F, Alonso R. Anaphylactic intraoperative reaction to latex. *Contact Dermatitis* 1995; 32: 305-307.
6. Hodgson C A, Andersen B D. Latex allergy: an unfamiliar cause of intraoperative cardiovascular collapse. *Anaesthesia* 1994; 49: 507-508.
7. McKinstry L J, Fenton W J, Barrett P. Anaesthesia and the patient with latex allergy. *Can J Anaesth* 1992; 39: 587-589.
8. Ownby D R, Tomlanovich M, Sammons N, McCullough J. Anaphylaxis associated with latex allergy during barium enema examinations. *Am J Roentgenology* 1991; 156: 903-908.
9. Lear J T, English J S C. Anaphylaxis after hepatitis B vaccination. *Lancet* 1995; 343: 1249.

10. Beuers U, Baur X, Schraudolph M, Richter W O. Anaphylactic shock after game of squash in atopic woman with latex allergy. *Lancet* 1990; 335: 1095.
11. Turjanmaa K, Reunala T. Incidence of positive prick test to rubber protein. *Contact Dermatitis* 1990; 23: 279.
12. Turjanmaa K. Incidence of immediate allergy to latex gloves in hospital personnel. *Contact Dermatitis* 1987; 17: 270-275.
13. Arellano R, Bradley J, Sussman G. Prevalence of latex sensitization among hospital physicians occupationally exposed to latex gloves. *Anesthesiology* 1992; 77: 905-908.
14. Iacobelli A, McCullough J, Ownby D. The prevalence of latex allergy in high risk medical personnel. *J Allergy Clin Immunol* 1993; 91: 216.
15. Lagier F, Vervloet D, Lhermet I, Poyen D, Charpin D. Latex allergy in nurses. *J Allergy Clin Immunol* 1992; 90: 319-322.
16. Charous B L, Hamilton R G. Occupational latex exposure: characteristics of contact and systemic reactions in 47 workers. *J Allergy Clin Immunol* 1994; 94: 12-18.
17. Zaza S, Reeder J M, Charles L E, Jarvis W R. Latex sensitivity among perioperative nurses. *AORN Journal* 1994; 60: 806-812. (erratum 1995; 61: 19).
18. Holm J O, Wereide K, Halvorsen, Thune P. Allergy to latex among hospital employees. *Contact Dermatitis* 1995; 32: 239-240.
19. Berkly Z, Luciano J, James W. Latex gloves: a survey of the US Army dental corps. *JAMA* 1992; 268: 2695-2697.
20. Mansell P, Reckless J P, Lovell C R. Severe anaphylaxis reaction to latex rubber surgical gloves. *Br Dent J* 1995; 178: 86-87.
21. Wrangsjo K, Osterman K, Van Hage-Hamsten M. Glove-related among operating theatre and dental care unit personnel (II). Clinical examination, tests and laboratory findings indicating latex allergy. *Contact Dermatitis* 1994; 30: 139-143.
22. Salkie M L. The prevalence of atopy and hypersensitivity to latex in medical laboratory technologists. *Arch Pathol Lab Med* 1993; 117: 897-89.
23. Konz K R, Chia J K, Kurup V P, Resnick A, Kelly K J, Fink J N. Comparison of latex hypersensitivity among patients with neurologic defects. *J Allergy Clin Immunol* 1995; 95: 950-954.
24. Pittman T, Kiburz J, Gabriel K, Steinhardt G, Williams D, Slater J. Latex allergy in children with spina bifida. *Pediatr Neurosur* 1995; 22: 96-100.
25. Kelly J, Pearson M L, Kurup V P, Havens P I, Setlock M A, Butler J C, Slater J E, Grammer L, C, Resnick A, et al. A cluster of anaphylactic reactions in children with spina bifida during general anesthesia: epidemiologic features, risk factors and latex hypersensitivity. *J Allergy Clin Immunol* 1994; 94: 53-61.
26. Alenius H, Kurup V, Kelly k, Palosuo T, Turjanmaa K, Fink J. Latex allergy: frequent occurrence of IgE antibodies to a cluster of 11 latex proteins in patients with spina bifida and histories of anaphylaxis. *J Lab Clin Med* 1994; 123: 712-720.
27. Gold M, Swartz J S, Braude B M, Dolovich J, Shandling B, Gilmour R F. Intraoperative anaphylaxis: an association with latex sensitivity. *J Allergy Clin Immunol* 1991; 87: 662-666.
28. Moneret-Vautrin D A, Mata E, Gueant J L, Turgeman D, Laxenaire M C. High risk of anaphylactic shock during surgery for spina bifida. *Lancet* 1990; 335: 865-866.
29. Warpinski J R, Folger J, Cohen M, Bush R K. Allergic reaction to latex: a risk factor for unsuspected anaphylaxis. *Annals Proceedings* 1991; 12: 95-102.
30. Champion R H, Parish W E. Atopic Dermatitis. In: Rook, Wilkinson, Ebling (eds): *Textbook of dermatology*, 5th edition. London: Blackwell; 1992: vol 1, p.590.
31. Stoetling R K. Allergic reactions during anaesthesia. *Anaesth Analg* 1983; 62: 341-356.
32. Fisher MMCD. The diagnosis of acute anaphylactoid reactions to anaesthetic drugs. *Anaesth Intensive Care* 1981; 9: 235-241.
33. Fisher M. Intradermal testing after anaphylactoid reactions to anaesthetic drugs: Practical aspects of performance and interpretation. *Anaesth Intensive Care* 1984; 12: 115-120.
34. Roy C A, Barton C R. Intraoperative latex anaphylaxis compounded by atracurium sensitivity: a case report. *AANA Journal* 1991; 59: 399-404, (erratum 1991; 59: 504).
35. McCormack D R, Heisser A I, Smith L J. Intraoperative vecuronium anaphylaxis compounded by latex hypersensitivity. *Ann Allergy* 1994; 73: 405-408.
36. Hanifin J M, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm acta-venereologica* 1980; suppl 92: 44-7.
37. Pepys J, Pepys E O, Baldo B A, Whitwam J G. Anaphylactic/anaphylactoid reactions to anaesthetic and associated agents. Skin prick tests in aetiological diagnosis. *Anaesthesia* 1994; 49: 470-475.

Address:

B. B. Tan
 North Staffordshire Hospital
 Central Out-patients
 Hartshill Road, Stoke-on-Trent, ST4 7PA
 UK

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.