Anaphylactic reactions during surgical and medical procedures

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The most common agents that are responsible for intraoperative anaphylaxis are muscle relaxants. However, latex accounts for a significant number of these reactions, and the incidence of intraoperative anaphylaxis caused by latex is increasing. It is now probably the second most important cause of intraoperative anaphylaxis. Following muscle relaxants and latex are probably antibiotics and anesthesia induction agents. Other agents that are responsible include colloids, opioids, and radiocontrast material. However, they account for less than 10% of all reactions. The clinical manifestations of intraoperative reactions differ from those of anaphylactic reactions outside of anesthesia. Cutaneous manifestations are far less common; cardiovascular collapse may be more common. The diagnosis can be made more difficult because patients cannot express symptoms. There is a paucity of cutaneous findings; the patient is draped, and concomitantly administered drugs may alter the manifestations. These additional drugs can also complicate therapy. There are populations who are at-risk for anaphylaxis to latex during surgical procedures: individuals with a genetic predisposition (atopic individuals), individuals with increased previous exposure to latex (eg, anyone who requires chronic bladder care with repeated insertion of latex catheters or chronic indwelling catheters), health care workers who are exposed to latex mainly by inhalation, and possibly patients who have undergone multiple surgical procedures and therefore have been exposed to latex intravascularly and by catheterization on a number of occasions. It has been shown that pretreatment with antihistamines and corticosteroids that are used successfully for the prevention of reactions to radiocontrast material are not as effective in the prevention of anaphylactic reactions to latex. Therefore, the major emphasis has been on prevention. The key elements of prevention include an adequate history, testing for latex allergy in high-risk patients, preadmission measures, and the establishment of a "latex-free environment" while the individual is hospitalized. This is particularly important in the operating and recovery rooms. (J Allergy Clin Immunol 2002;110:S64-9.)

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0091-6749/2002 $35.00 + 0 **1/0/124970**
doi:10.1067/mai.2002.124970

Key words: *Anaphylaxis, anaphylactoid reactions, latex, muscle relaxants, anesthesia*

This article was composed as a part of a symposium on latex allergy. Therefore the impetus of the article was to explore the role of latex in anaphylactic reactions during anesthesia and medical procedures. However, latex is by no means the only and actually not the major cause of such reactions. Thus, the early portion of the article will be devoted to anaphylactic reactions during anesthesia and medical procedures in general, and the latter portion will be delegated specifically to latex allergy in this regard, emphasizing the clinical features that can distinguish latex anaphylaxis from anaphylaxis caused by the administration of medications and the preventive measures that can be taken to avoid latex reactions.

INCIDENCE

The prevalence of anaphylactic reactions during the perioperative period and during medical procedures overall has been defined poorly. There are little data that assess the incidence of such reactions outside hospitals, but several series have evaluated the incidence during general anesthesia.[1-12] In an early report from Australia, Fisher and Moore,[9] in 1981, found an incidence of between 1 in 5000 and 1 in 25,000 with a mortality rate of 3.4%. Later, in an extended series that was reported in 1993, Fisher and Baldo[2] found an estimated incidence of anaphylaxis between 1 in 10,000 to 1 in 20,000 in Australia. An early series that was reported from France by Hatton et al[10] in 1983 found 1 severe anaphylactoid reaction occurring for every 4500 cases of general anesthesia. A more recent series from France by Laxenaire[3] discovered an incidence of 1 per 13,000 operative procedures and a mortality rate of 6%. Clark et al[11] found that drugs were implicated in 4.3% of deaths that occurred during anesthesia in the United Kingdom and were reported in 1975. More recent but smaller studies have been published from New Zealand,[4] the United Kingdom,[5] and the United States[6,7] that show similar incidences.

It is interesting to note that, as in other forms of allergic reactions, the prevalence of sensitization is higher than the incidence of reactions. For example, Porri et al[13] studied the incidence of skin test reactivity to muscle relaxants in the general population. They found that 9.3% of 255 subjects had positive skin tests to muscle relaxants, an incidence that far exceeds the incidence of anaphylaxis on the administration of these drugs during anesthesia.

AGENTS RESPONSIBLE FOR ANAPHYLAXIS DURING ANESTHESIA AND MEDICAL PROCEDURES

A list of the most common agents that are responsible for anaphylactic reactions during anesthesia and medical procedures is seen in Table I. Without a doubt, the most common agents that are responsible for anaphylactic episodes are muscle relaxants. In a recent report from France by Mertes and Laxenaire,[12] muscle relaxants accounted for 61.6% of anaphylactic reactions in 452 patients who underwent general anesthesia. This is in keeping with other reports that demonstrate a range of 50% to 70%.[3,5-7,14,15]

In France, Laxenaire,[3] in an earlier report, found that muscle relaxant–induced anaphylaxis occurred in an estimated 1 in 6500 anesthesias. In the series by Mertes and Laxenaire,[12] the most commonly incriminated agent was vecuronium bromide (28.8%) followed by atracurium besylate (23.7%), and suxamethonium chloride (23.5%). However, in previous series,[16-18] suxamethonium was incriminated most commonly.

The next most frequent agent that accounts for anaphylactic events during surgical procedures is latex. The incidence of anaphylactic reactions to latex during anesthesia and medical procedures has been increasing over the last decade. However, the first report of an IgE-mediated reaction to latex appeared in the German literature in 1927.[19] The reaction occurred during a dental procedure. In this index case, the patient was a 48-year-old woman in whom urticaria and angioedema developed after the insertion of a dental prosthesis that contained rubber. On removal of the prosthesis, symptoms subsided and then returned on reinsertion. Latex was determined to be the culprit after skin testing and an oral challenge. The first English language report of latex allergy occurred in 1979.[20] The first 2 cases of intraoperative anaphylactic reactions were reported by Turjanmaa et al[21] in 1984. But intraoperative latex anaphylaxis was probably not recognized as an important problem until 1988 after the report of 2 cases of intraoperative anaphylaxis in children with spina bifida.[22] As of 1992, the Food and Drug Administration had received 1100 reports of allergic or anaphylactic reactions that occurred during medical procedures. Most of these cases involved latex gloves and barium enema catheters. Fifteen deaths, all caused by barium enema catheters, had been reported by that time.[23] By 1996, latex was reported to account for approximately 10% of anaphylactic reactions during surgery[24] and, by 2000, had been reported to account for as much as 16.6% of these reactions.[12] Thus, muscle relaxants and latex account for most reactions during anesthesia.

After these 2 causes, in frequency, are antibiotics and then induction agents.[12] Other agents including colloids, opioids, radiocontrast probably account for less than 10% of all reactions.[9,10,12]

TABLE I. Examples of the most common agents that cause anaphylaxis during anesthesia and medical procedures

Muscle relaxants
Succinylcholine (suxamethonium)
Atracurium
Vecuronium
Pancuronium
Induction agents
Barbiturates
Etomidate
Propofol
Narcotics
Fentanyl
Meperidine
Morphine
Colloids for intravascular volume expansion
Antibiotics
Radiocontrast
Blood products
Latex
Others
Protamine
Mannitol

SIGNS AND SYMPTOMS

It is worthwhile to mention the signs and symptoms of anaphylaxis that occur during anesthesia because these differ from those signs and symptoms that occur during anaphylaxis that is not associated with anesthesia. Table II highlights some of these differences. This Table shows a comparison of an analysis of 5 series of anaphylaxis cases (1158 cases) that were not associated with anesthesia[25-29] with 583 anesthesia-associated episodes of anaphylaxis and anaphylactoid events.[3]

It should be noted that the figures in this Table are not precise, in that different series report symptoms and signs in different manners and some exclude symptoms and signs that are reported by others. For example, dizziness (a symptom) was reported in the nonsurgical cases, whereas this could not be detected in those cases that were associated with surgical procedures.

In addition, the surgical episodes could be classified by mechanism, which separated the episodes that were truly anaphylactic (IgE-mediated) from those episodes that were anaphylactoid (eg, non–IgE-mediated histamine release). Of importance is the fact that there were distinct differences between the anaphylactic and the anaphylactoid events. As can be seen from Table II, the frequency of cutaneous manifestations was higher in anaphylactoid events, although the cardiovascular manifestations and bronchospasm were more frequent in anaphylactic events.[3] Also of interest is the fact that anaphylactic events were, in this series, more severe as a rule than anaphylactoid reactions.[3]

Several other salient points can be gleaned from the information in Table II. First, cutaneous manifestations are more common in episodes that are not related to anesthesia. This might be explained by the fact that patients are draped during the anesthesia process and cannot complain of cutaneous symptoms (such as pruritus) or sense a flush. On the other hand, cardiovascular collapse

TABLE II. Comparison of clinical manifestations of anaphylaxis that occur during surgical procedures, with episodes not surgically related*

		Surgical (%)	
Manifestations	**Nonsurgical (n = 1158)(%)**	**Anaphylaxis (n = 307)**	**Anaphylactoid (n = 177)**
Cutaneous†	98	75.6	86
Cardiovascular			
Hypotension	21	18.0	20
Cardiovascular collapse	—‡	49.0	12
Dizziness, syncope	31	—‡	—‡
Respiratory			
Wheeze, bronchospasm	53	41.9	25
Death	0	<1.0§	0

*Summarized from references 3 and 25 to 29.
†Flush/erythema, urticaria, angioedema.
‡Not reported.
§Two deaths.

TABLE III. Clinical features that suggest latex as a cause of perioperative anaphylaxis

There is a delay in onset of reaction; reaction occurs during maintenance anesthesia and not induction.
Most common setting is gynecologic and obstetric procedures.
May follow oxytocin injection.

TABLE IV. Groups that are at risk for anaphylaxis to latex during surgical or medical procedures

Chronic bladder care
Neural tube defects
Spina bifida
Myelomeningocele
Spinal cord trauma
Urogenital malformations
Neurogenic bladder
Health care workers (greatest for operating room)
Patients with multiple surgical procedures
Atopic individuals

appears to be more common during surgical procedures than during nonsurgical anaphylaxis. There were no deaths in the series of anaphylaxis and 2 deaths in the surgical series, both occurred in the anaphylactic group. It is noteworthy that there are several features of intraoperative anaphylactic events that can make the diagnosis particularly difficult. On occasion there may be only a single manifestation, such as cardiovascular collapse or airway obstruction. The patient is draped, and there is often a paucity of cutaneous findings. There is also, of course, the absence of symptoms, which leaves signs as the only clues to the existence of a reaction. Finally, the use of multiple drugs during the procedure cannot only alter the manifestations but also complicate therapy.

There are some distinguishing features that point toward latex as a cause of an anaphylactic reaction during surgical procedures (Table III). Most episodes of surgical anaphylaxis occur during the induction procedure when muscle relaxants, sedatives, and opiates are administered. However, latex reactions occur during maintenance anesthesia, usually exhibiting a delay of anywhere from 30 to 60 minutes. The most common setting for latex anaphylaxis in surgical procedures may be obstetric and gynecologic procedures.[30] The reason for this is unclear but may be related to the observation that sensitization to latex has been reported to occur more frequently in women.[31] Finally, latex reactions can follow the injection of oxytocin during obstetric and gynecologic procedures. It has been hypothesized that this phenomenon is the result of sudden uterine contraction, produced by oxytocin, which causes the release of latex particles that are deposited in the uterus into the bloodstream. Except for these features, latex reactions are similar in manifestation to those reactions that are caused by other agents that are encountered during surgical and medical procedures.

As noted, the most frequent type of surgical procedures that are associated with reactions to latex may be those related to obstetric and gynecologic procedures. They have been reported to account for approximately 50% of all reactions caused by latex. The next most frequent are those reactions that occur during abdominal operation, which represent approximately 20% of cases, and during orthopedic operation, which accounts for 10% of cases.[30]

It should be clearly noted that latex anaphylactic reactions are not limited to surgical procedures but can occur during a number of other medical procedures. In fact, the index cases that alerted the Food and Drug Administration to the risk of latex reactions were originally reported to be caused by contact with latex tips that were used during barium enemas. Ownby et al[32] reported a series of such cases in 1991. In addition, a number of other medical and dental procedures have caused latex-induced anaphylactic events, including the insertion of catheters, dental procedures, and childbirth.[33]

POPULATIONS AT RISK FOR ANAPHYLAXIS TO LATEX DURING SURGICAL AND MEDICAL PROCEDURES

A number of groups of individuals are at risk for anaphylactic reactions to latex during surgical and medical procedures (Table IV). The at-risk populations can be

Attachment A
Policy Memorandum 00-65

1. Have you ever had an allergic reaction to latex (rubber) devices/products?
   Yes No

2. Has your doctor or dentist ever told you that you have an allergy to latex (rubber) products?
   Yes No

   If yes, what were you told?_____

3. Do you have a medical condition/abnormality (i.e., spina bifida, myeloma, tracheoesophageal fistula, and bladder dysfunction) that has caused you to be exposed to a great number of latex supplies?
   Yes No

4. Have you had a reaction (i.e., redness, swelling, watery eyes, breathing difficulty) to the following sources of latex (rubber)?

	Yes	No		Yes	No
Balloons			Latex Birth Control Devices		
Rubber Gloves			Dental Cofferdams		
Hot Water Bottles			Face Masks (latex/rubber)		
Rubber Bands			Elastic Bandages		
Foam Pillows			Elastic Cuffs, Waistbands		
Baby Supplies			Ostomy Bags		
Belts, Bras			Shoe wear		
Suspenders			Rubber Grips		
Other					

After handling latex (rubber) products, have you ever had any of the following?

	Yes	No
Difficulty Breathing		
Chapping of Hands		
Runny Nose		
Redness		
Swelling		
Hives		
Itching		
Other		

If any question is answered "Yes," identify as Latex Sensitive and notify primary provider.

FIG 1. Latex allergy questionnaire.[44]

TABLE V. Measures to take to prevent latex anaphylaxis during medical procedures

Complete a medical history to establish the existence of latex allergy.
Test for latex allergy in high-risk patients or patients with a positive medical history.
Establish preadmission measures.
Establish a "latex-free" hospital room.
Create a "latex-free" treatment cart.
Institute latex reduction measures in the operating room or treatment room and the recovery room.
Pretreat with prednisone and an H_1 receptor antagonist.*

*Although pretreatment has not proved to be effective in the prevention of reactions to latex, there is still a theoretic rationale for its use, and it might therefore be considered.

TABLE VI. Examples of the contents of a latex-free cart

Glass syringes
Ampules
Tubing without ports (taped ports)
Stopcocks
Non-latex stethoscope
Non-latex gloves
Non-latex breathing system
Neoprene bags
Plastic masks
Non-latex Ambu
Uncuffed polyvinyl chloride endotracheal tube
Dermacil
Disposable non-latex blood pressure cuffs
Webril tourniquets

TABLE VII. Operating, treatment, and recovery room procedures

Latex-free breathing system
Non-latex bite blocks
Non-latex electrocardiogram and pulse oximetry leads
Latex-free bandages, tape, tubing
Latex-free gloves
Non-latex catheters

TABLE VIII. Suggested concentrations for skin testing to selected drugs that could be responsible potentially for intraoperative anaphylaxis

	Concentration (mg/mL)		
Medication	**Moscicki et al[6]**	**Fisher[45]**	**Vervloet et al[46]***
Succinylcholine (suxamethonium)	0.02	0.05	0.1
Pancuronium	0.002	0.002	0.2
Vecuronium	—	—	0.4
Alcuronium	—	0.005	0.05
Tubocurarine	0.0003	0.001	0.003
Gallamine	—	0.04	0.2
Metocurine	0.002	—	—
Methohexital	0.1	0.1	—
Protamine	—	0.001	—
Thiopental	0.20	0.25	—
Thiamylal	0.01	—	—
Rocuronium	—	—	0.1
Mivacurium	—	—	0.002

*Defined by authors as the concentration that gives negative results for all control subjects.[45]

grouped into those individuals with genetic predisposition (atopic individuals) and those individuals with increased exposure to latex (eg, anyone who requires chronic bladder care with the repeated insertion of latex catheters or chronic indwelling catheters, health care workers exposed to latex mainly by inhalation [especially those who work in an operating room], and questionably patients who have undergone multiple surgical procedures and therefore have been exposed to latex intravascularly and by catheterization on a number of occasions). When the genetic predisposition is combined with exposure, the risk is greatest.

The incidence of latex sensitivity in the general population ranges from 0.8% to 6.5%,[34] whereas the incidence of latex sensitivity in patients who require chronic bladder care (eg, individuals with bladder exstrophy and spina bifida) has been reported to be as high as 72%.[35]

Health care workers, because of regular exposure to latex, are also a group that is at-risk. This appears especially true for those health care workers who work in operating rooms where the ambient air level of latex is the highest. For example, latex allergy in physicians who are exposed to latex and who are not anesthesiologists has an incidence of approximately 10%, whereas the prevalence among anesthesiologists is approximately 12%.[36] Similar findings were reported by Turjanna,[37] who tested 512 hospital employees for immediate hypersensitivity to latex and found the highest prevalence in those who worked in operating rooms where latex gloves were used daily. Nurses who work in operating rooms have a similar prevalence of latex sensitivity that ranges from 6.9%[38] to 10.7%.[39] Nurses who work in labor and delivery are also at high risk; in 1 study, nurses who worked in labor and delivery had a sensitization rate of 13.6% versus an incidence of 6.3% for operating room nurses.[40] In this study, medical surgical nurses had an incidence of 8.2%, and emergency room nurses had an incidence of 10.4%.[40]

Atopy also clearly increases the risk for sensitization. Hospital physicians who have atopy have a 24% incidence of latex sensitivity.[36]

Dental and laboratory workers, as well as medical personnel, are also at risk for latex reactions.[4]

PREVENTION

There are well-established procedures that were designed to prevent anaphylactic reactions to latex during medical and surgical procedures.[33] Because pretreatment with antihistamines and corticosteroids that have been used successfully for the prevention of reactions to radiocontrast in predisposed patients does not appear to protect against life-threatening intraoperative anaphylactic reactions to latex,[41-43] preventive measures have evolved to create a "latex-free environment."

The effectiveness of the latex-free environment is predicated first on the establishment of a diagnosis of latex allergy or the potential for an anaphylactic reaction to latex during the medical procedure. Thus, the course of prevention of latex reaction begins with an adequate medical history, followed by testing when indicated and then the institution of environmental control measures (Table V). The medical history is essential to establish whether a patient is at high risk. Several questionnaires have been designed to identify high-risk patients. An example of such a questionnaire is seen in Figure 1, which was taken from a policy memorandum (00-65) issued August 21, 2000, from the Department of Veterans Affairs, and obtained from the Medical Center Veteran's Hospital affiliated with the University of Tennessee College of Medicine.[44] If this questionnaire indicates that an individual is at risk, testing for latex allergy can be performed when the attending physician deems it to be appropriate.

If it is decided that a patient is at risk, then precautionary measures begin before admission. The facility should be prepared to care for the individual who is allergic to latex. A multidiscipline task force should address the issues of risk management. Individuals who are known to be at risk should be educated regarding avoidance of latex products in their daily lives. Before these individuals are admitted to a hospital, arrangements should be made for a private room, and all natural latex rubber items should be removed from the room before admission. The room should be cleaned by personnel who wear synthetic gloves. Sharps containers should be replaced; wall-mounted blood pressure devices should not be used; and

the bed and all patient contact surfaces should be wiped down to remove residual glove powder. Labels should be placed on the bed, on the room door, and on the patient's armband to identify the patient's latex allergy status.

The hospital should have a latex-free cart available (Table VI). All urology and lithotripsy equipment should be reviewed for latex content. Silicone-coated urinary catheters are not safe for patients with latex allergy. One hundred percent silicone or other synthetic catheters should be used instead. The pharmacy should have a latex-free protocol for medications.

In addition, of course, latex prevention measures should be taken in the operating or treatment room and in the recovery room (Table VII). The most important measure in this regard is the use of non-latex gloves. In addition, surgical procedures for a latex-sensitive patient should be performed as the first case in the morning so that the lowest possible content of latex-coated powder is in the ambient air.

Experience with these measures has demonstrated that patients who are allergic to latex can undergo surgical and medical procedures without reaction.

In closing, it should be remembered that latex is not the most common cause of intraoperative anaphylaxis. The allergist sees the patient after the event, most often to identify the culprit so that there is no recurrence during a repeat procedure. This requires a detailed review of the operative record to obtain a list of the drugs used. Fortunately, there are skin test protocols that are available for many of the agents that are administered. Representative skin test regimens from 3 sources are given in Table VIII.[8,45,46]

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