

## Article: "Is Occupational Latex Allergy Causing Your Patient's Asthma?"

**ABSTRACT:** Given the prevalence of latex allergy in health care workers and others who wear latex gloves, it is prudent to maintain a high index of suspicion in patients with occupational exposure. In the United States, confirmation of suspected latex allergy relies on serologic tests that are significantly less sensitive than skin prick test methods that are available in Canada and Europe. Specific inhalation challenge is the gold standard for the diagnosis of occupational asthma, but it is not commonly available. Successful management of affected patients relies on cessation of exposure. Workers who are not exposed to contaminated fluids should use nonlatex gloves. When latex gloves are needed, only nonpowdered nonsterile gloves and/or nonpowdered or low-protein powdered latex surgical gloves should be used. (J Respir Dis. 2002;23(4):250-256)

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For more than a century natural rubber latex, commonly referred to as "latex," has been widely used in medical devices because of its attractive combination of properties that include strength, flexibility, tear resistance, elasticity, and barrier qualities. The development of latex gloves by the latter half of the 19th century was hastened by the ease of manufacturing dipped latex products and the superior tactile qualities of the resultant product.

Joseph Bloodgood, the lesser-known associate of the noted surgeon William Halstead, played a major role in popularizing surgical latex gloves with his persuasive demonstration of their benefits. In the late 1980s, the advent of "universal precautions" expanded the use of nonsterile (examination) latex almost exponentially?in 1999, more than 15 billion pairs of gloves were sold in the United States.

During most of the last century latex was viewed as completely safe; the only notable problem was the increased prevalence of contact dermatitis with latex glove use. This difficulty was rarely caused by latex itself?it was due to an allergic contact dermatitis sensitivity to a chemical additive used in manufacturing or a nonspecific irritation associated with glove use. Hence, about 10 years ago, reports of anaphylactic reactions to latex (including some deaths) were surprising.

Two distinct high-risk groups were initially identified: children with spina bifida (although later it became apparent that any infant who underwent frequent surgical procedures was at risk) and patients who had undergone radiologic examinations that used latex rubber barium enema retention balloons. Fortunately, institution of prophylactic safety measures has virtually eliminated serious reactions in these patients.

In this article, we will discuss the sources of latex exposure and the diagnosis and management of latex allergy and asthma.

#### Risk factors for allergic sensitization

In the early 1990s, reports of allergic reactions in health care workers generated questions about the risks of occupational disease associated with long-term exposure to latex products. (1) Are health care workers and others who wear latex gloves at increased risk for becoming sensitized to latex? Is this sensitization clinically relevant: do contact hives, rhinoconjunctivitis, asthma, and anaphylaxis occur more frequently in exposed persons than in non-exposed persons? Are all latex products equally responsible for causing symptoms? Most important, since the diagnosis of occupational allergy and asthma implies significant human, legal, and economic costs, how and at what cost can a safe workplace be established?

Some of the answers to these questions have become available recently through an impressive international effort to delineate the nature of latex allergy. Studies from several groups working independently have demonstrated remarkably consistent findings concerning the occupational nature of this problem. (2-4)

Although atopic persons are more likely to become allergic to latex than nonatopic persons, the key determinant of latex sensitization is exposure. Population prevalence studies that have used the skin prick test, the most accurate assessment tool, have reported positive test results in 5% to 12% of latex-exposed workers. (5-7) Nearly half of these sensitized workers reported a history of allergic reactions.

In one study, 50% of allergic workers with no history of asthma experienced an asthmatic response during a ?glove handling? inhalation challenge. (8) This suggests that long-term exposure to latex aerosol can provoke lower airway inflammatory responses and asthma. Observed rates of 2% to 10% for occupational asthma (OA) in workers who had long-term exposure justify concern. (7,9,10) However, only 2% to 3% of nonexposed atopic persons and only about 1% of the general population have positive skin test results. More important, allergic symptoms are rarely reported in these groups. (2,5,11)

The relationship of latex sensitization and allergy to the duration and extent of exposure has been examined in several studies. Three of these studies examined the effects of latex exposure on ?new job entrants,? a group particularly relevant to understanding the nature of occupational risk. (12-15)

Tarlo and colleagues (12) reviewed cross-sectional rates of latex sensitization and allergy in University of Toronto Dental School students and faculty. None of the first- and second-year dental students who were tested were allergic. However, 5% of third-year and 10% of the fourth-year students had become sensitized. A quarter of faculty who were tested were allergic, and 10% had asthma (Figure).

Levy and associates (13) performed a similar study on dental students in London and Paris. None of 86 preclinical students had a positive skin test result. However, of the 189 graduating students, 11(6%) were allergic to latex.

An impressive prospective study at the University of Montreal and McGill University assessed the incidence of occupational allergy and asthma in more than 750 apprentice workers in 3 diverse categories: animal health technology, pastry- making, and dental hygiene technology. (14,15) On entry, the prevalence of latex allergy was

insignificant in all 3 groups; however, during the course of the study, striking differences emerged.

Among the dental hygiene technology apprentices, who used latex gloves regularly, latex allergy became more widespread. Over 32 months, the cumulative incidence in this group for latex sensitization was 6.4% and for OA was 4.5%. (15) Underlining the potency of latex as an aeroallergen, the likelihood of latex sensitization in the dental hygiene technology apprentices was greater than the likelihood of animal-derived allergen sensitization in the animal health technology apprentices. (15)

Levy and colleagues (13) noted that latex allergy was not evenly distributed among the dental students but, rather, was confined to those who had used powdered latex gloves. In fact, none of the 93 graduating dental students who had used only powder-free protein-poor gloves was allergic to latex.

Baur and associates (16) reported analogous findings in a study of airborne latex aeroallergen exposure. They screened 145 persons and performed aeroallergen sampling in 32 hospital and operating rooms and physicians' offices. (16) Latex aeroallergen concentrations varied widely, ranging from undetectable levels to 205 ng/[m.sup.3]. Fifteen percent of the workers showed evidence of latex allergy; however, all of the persons who were sensitized had worked in areas where the aerosol concentrations were at least 0.6 ng/[m.sup.3]. This suggests that as with other industrial and indoor allergens, such as dust mites, a threshold for latex aeroallergen may be associated with the development of sensitization and subsequent symptoms.

#### Sources and routes of exposure

Latex exposure takes place either through direct skin contact or via inhalation. The first route of exposure may sensitize those who wear latex gloves regularly, especially persons with contact dermatitis whose normal barrier function of the skin has been disturbed. Numerous aerosol sampling studies have found appreciable levels of aeroallergen in medical settings, with concentrations ranging from less than 1 to more than 300 ng/[m.sup.3]. It is worth noting that levels of this magnitude are quite similar to the concentrations of other aeroallergens, including laboratory and domestic animal proteins, flour dust, and papain, which are known to induce OA. (17)

From where does latex aeroallergen arise? In the medical setting, the generation of latex aeroallergen is directly dependent on the active use of powdered latex gloves. (18-20) When nonpowdered latex or non-latex gloves are substituted for powdered latex gloves, latex aeroallergen levels predictably disappear, even when no other preventive measures are taken. In rooms without carpeting, latex aerosol levels become undetectable within hours. (18,21) The presence of carpeting and/or other repositories, such as fabric upholstery, appears to delay, but not prevent, this fall in latex aeroallergen levels.

It is worth emphasizing that the use of powdered latex gloves exposes not only the wearer to latex aerosol but coworkers and patients as well. We have previously reported results of an investigation into the sources and dispersion of latex aeroallergen in a multipractitioner dental office. (21) This study was prompted by findings of worsening asthma in a dental assistant with latex allergy who maintained careful adherence to personal measures of avoidance.

The initial aeroallergen sampling confirmed our suspicions that latex aerosol had dispersed into her work area (12 to 14 ng/[m.sup.3]) from other areas where powdered latex gloves were still in use. Latex aerosol was found in the patient waiting area (7 ng/[m.sup.3]) and in all the other operatories, hygiene rooms, and laboratories sampled (14 to 90 ng/[m.sup.3]) An initial attempt to substitute nonpowdered latex gloves throughout the office was effective in reducing concentrations in her work area to below 5 ng/[m.sup.3]. Persistent elevation of aeroallergen levels in 1 operatory was noted and finally was explained by the discovery of continued, but unannounced, use of powdered gloves. Ultimate conversion to the use of 'lightly powdered,' lower-allergen gloves in this area led to effective

elimination of latex aerosol in all but the rooms where such gloves were used.

Taken together, these multiple independent observations strongly suggest that implementation of appropriate glove procurement policies may eliminate latex aerosol and prevent both sensitization of glove wearers and inadvertent secondary exposure of patients with latex allergies. (22)

#### Presentations of latex allergy

Typically, initial symptoms of latex allergy are contact reactions, such as urticaria or acute erythema with pruritus, that occur during a glove distribution. Some persons manifest an acute dyshidrotic reaction similar to a protein contact dermatosis. The diagnosis of contact dermatitis should be considered in patients who have rashes that persist beyond several hours or that are chronic. In our experience, most of these patients have had a nonspecific irritant dermatitis. However, cases of allergic contact sensitivity to rubber accelerators, such as thiuram, are not infrequent, and patch testing can provide a definitive diagnosis. You should be aware that the presence of contact dermatitis, whether due to contact allergy or nonspecific irritation, does not preclude the development of IgE-mediated latex allergy.

A broad spectrum of respiratory complaints are attributable to latex allergy. Some patients voluntarily report worsening symptoms and connect them with on-the-job exposure. We believe that this is true of patients with upper respiratory tract symptoms. Sneezing, ocular tearing and itching, severe rhinor-rhea, and nasal stuffiness are common and may be indistinguishable from acute seasonal allergic rhinitis. When the patient is unaware that latex is causing or contributing to discomfort, the possibility of latex allergy may be suggested by positive responses on a screening questionnaire.

Lower respiratory tract complaints may range from a classic syndrome of wheezing and shortness of breath occurring or worsening at work to chronic cough. Not uncommonly, the course of OA is insidious. Gradually worsening asthma may be missed or may not be recognized as a result of workplace exposure. Even patients with a history of other acute on-the-job symptoms, such as contact urticaria, cannot always identify the source of their asthma. Other concurrent occupational and nonoccupational exposures, such as exposure to domestic pets or to house dust mites, may add confusion. For these reasons, all patients with occupational latex allergy should have screening studies for coexisting ?silent? OA.

Chronic cough in a latex-allergic patient who has no evidence of air-way hyperreactivity may be due to eosinophilic bronchitis. (23)

#### Diagnostic considerations

Given the prevalence of latex allergy and OA in health care and glove-donning workers, it is prudent to maintain a high index of suspicion in patients with occupational exposure. Assessment for possible latex allergy is mandatory before any medical, dental, or surgical procedure that involves use of latex devices or gloves. Particularly, a history of current or previous occupational latex exposure and possible reactions should be sought. A history of contact or respiratory reactions induced by any of the following suggest the need for a more complete evaluation:

\* An exposure to powdered latex gloves.

\* Severe allergies to foods known to cross-react with natural rubber latex, such as avocado, banana, kiwi, and hazelnut.

\* Intraoperative anaphylaxis.

\* Reactions caused by commercial latex products, such as condoms and balloons.

Complaints of glove-associated hand eczema are so common among health care workers that they may be dismissed. However, contact dermatitis has been shown to be an independent risk factor for the development of latex allergy. (24,25) For this reason, patients should be questioned about changes in the nature of eczematous rashes?positive responses may indicate the conversion from contact dermatitis to IgE-mediated allergic disease. We use a simplified questionnaire at the initial patient consultation (Table).

Evaluation of occupational latex allergy and asthma is hindered by the lack of any FDA-approved skin test reagents. Some practitioners have used ?homemade? glove extracts as reagents, but because of the risk of systemic reactions, we recommend that this be done using only established protocols and appropriate reagent potency and stability testing with pooled anti-latex sera. (26)

An alternative approach uses any of the FDA-cleared serologic assays for detection of anti-latex IgE. Unfortunately, these assays perform below the standards of skin prick tests. (27) Thus, attempts to confirm a ?true? diagnosis in a patient with a convincing history of latex allergy may be confused by false-negative results.

When we have encountered patients with convincing histories who have no evidence of anti-latex IgE on serologic testing, we have used glove-wearing challenges to confirm or exclude the diagnosis. If possible, we use an ?offending? glove-brand sample obtained from the patient?s workplace. Initially, a single digit is gloved for 20 minutes. If no reaction occurs, the entire hand is moistened and gloved for an additional 20 to 30 minutes. Signs of urticaria or erythema with pruritus indicate a positive response. Care should be taken to look for reactions occurring up to 15 to 20 minutes after removing the glove.

Other variants of this procedure use ?prick through glove? or ?prick under glove? methods. All of these tests are limited by lack of standardization and risk acute systemic reactions. For this reason, some centers have patients don masks during testing to prevent concurrent inhalation of glove powders.

Skin testing and glove challenges should be done only when there is immediate access to full resuscitative equipment and trained staff. Since carpeting and upholstery may act as reservoirs of latex allergen, tests should take place only in noncarpeted rooms, which must be damp-mopped afterward. Hooded exposure chambers and laminar flow helmets have been used for testing at some centers, but these methods are experimental.

Confirmation of suspected latex OA requires objective evidence of latex allergy and bronchial hyper-reactivity or asthma plus demonstration of a causal relationship between the patient?s asthma and exposure to latex aeroallergen. Either pre- or post-bronchodilator studies or a methacholine challenge can provide acceptable evidence of reversible airway obstruction. As is the case with other industrial exposures, confirming the relationship between a patient?s asthma symptoms/signs and latex exposure may be challenging.

A recent report underlined the poor predictive value of combined clinical history and immunologic tests for purposes of confirming suspected OA. (28) For this reason, specific inhalation challenge is the gold standard for diagnosis. Currently, this is available at only a few research centers. In its place, workplace peak flow monitoring has been used, although lack of patient compliance and effort can compromise this approach.

ternatively, we have used supervised, reproducible spirometric monitoring before, during, and after work for confirmation of suspected asthma in health care workers. In cases of severe asthma, employees should be removed from the workplace, and challenges or serial monitoring should be postponed until the patient is stabilized.

## Impact on the patient

Symptoms of frequent or acute attacks of severe asthma or anaphylaxis or pervasive sensations of shortness of breath, chest tightness, and difficulty in breathing may be hard to assess in some patients. Most of these patients have significant histories of occupational exposure to latex and objective evidence of latex allergy. However, patient reports of acute or repeated attacks occurring in public places, such as shoe stores, libraries, restaurants, and gas stations, in the absence of an identifiable source of latex exposure are not well explained as an allergic reaction to latex.

Confusing symptoms and an absence of clearly defined triggers may tempt you to minimize the patient's distress or to attribute ambiguous symptoms to malingering. Malingering, however, is an uncommon diagnosis, particularly in persons who have had stable work histories and life situations and who have achieved professional accomplishments. More likely, the ubiquity of latex and the multiplicity of cross-reactive foods may create a state of hypervigilance.

Consider the possibility that previous "bona fide" acute reactions, including anaphylaxis, may lead to a state that is characteristic of anxiety reactions ("fight or flight response"). (29) It has been appreciated for some time that asthma provokes a high level of anxiety, (29,30) and the symptom overlap between panic and respiratory disease may confound diagnostic clarity.

Fear reactions resulting from suggestion, (31) social contagion, or experience with an aversive allergic event (32) may prompt the patient to establish conditioned responses (33) that eventually may lead to generalization to a whole class of similar stimuli. Conditioned fear responses that mimic latex allergy as pseudoallergic reactions (34) may even intensify allergic and asthmatic reactions. The effects of these anticipatory attacks can be self-reinforcing and lead to social withdrawal, including agoraphobia in some severe cases. The decrements in quality of life and sense of well-being in such patients cannot be overstated.

## Management

The cornerstone of successful management of occupational latex allergy and asthma is cessation of exposure. Since powdered latex gloves are the only significant source of workplace latex aeroallergen, workers who are not exposed to contaminated fluids, such as food handlers, should be provided exclusively with nonlatex gloves. Where latex gloves are used, only nonpowdered nonsterile gloves (examination gloves) should be used.

Sterile latex gloves are an uncommon cause of problems in nonsensitized persons. For this reason, use of low-protein powdered surgical gloves (less than 50  $\mu\text{g/g}$  of ASTM D5712) instead of nonpowdered gloves is acceptable if an ongoing assessment for the development of allergic reactions is maintained. (22) Because the cost of conversion is not appreciable, the sales of nonpowdered latex examination gloves have already surpassed the sales of powdered latex examination gloves. This appears to be the most likely explanation for the precipitous decline in new patient latex OA referrals seen at our center and reported by other tertiary referral institutions. (35) Moreover, the institution of appropriate glove precautions in the workplace has permitted the safe return to work of almost all of our latex-allergic employees.

Hand dermatitis, including contact dermatitis, should be treated aggressively with both topical corticosteroids and moisturizers. You should discourage the use of petroleum-based skin moisturizing products under latex gloves because they compromise the barrier properties of latex rubber. Persistent dermatitis despite treatment suggests the need for a change to nonlatex gloves.

Workers with contact urticaria or symptoms of occupational allergic rhinitis who have confirmatory skin or serologic tests must avoid latex exposure. The routine use of  $\beta$ -blockers by such patients is contraindicated,

since these agents may block therapeutic response to drugs used for treatment of anaphylaxis. Patients with seasonal or perennial rhinoconjunctivitis may benefit from intranasal corticosteroids. However, we ask patients to refrain from routine use of antihistamines so that the appearance of acute symptoms at work can be used as a warning signal.

Treatment of OA follows the standard guidelines for nonoccupational asthma. With persistent asthma symptoms, use of inhaled corticosteroids, sometimes at high doses or supplemented with an initial burst of oral corticosteroids, is required. The addition of other asthma therapy, including long-acting bronchodilators, leukotriene receptor antagonists, and theophylline, may be helpful and should be considered on a patient-by-patient basis. Since cough frequently accompanies latex OA, dry-powder inhalers are often better accepted by patients.

Other contributing factors to asthma, such as sinusitis, gastro-esophageal reflux disease, vocal cord dysfunction, and other allergic exposures, should be sought diligently and treated. Despite aggressive treatment and cessation of exposure, asthma may persist for months or years after a patient has resigned from a job.

It is essential to appreciate the psychological impact of a diagnosis of latex OA. Workers who are unable to maintain their current profession may have to cope with significant financial stresses and a threatened sense of self-esteem. For those whose primary identification is with their job (?!?m an ICU nurse?), the diagnosis of latex allergy can mean ?the loss of life as you know it.? Referral to a psychologist or mental health practitioner with expertise in treating persons with chronic illness and an understanding of latex allergy can help restore a patient?s quality of life and promote a healthier adaptation to his or her circumstances. Table ? Simplified latex allergy questionnaire Circle Y or N I. Risk factor assessment: 1. Exposure history: A. Are you a health care worker or do you wear gloves regularly? Y N B. Do your fellow workers wear latex gloves regularly? Y N C. Did you undergo frequent surgeries or invasive medical procedures during infancy? Y N 2. Do you have a history of ?hay fever? or other common allergies? Y N 3. Do any foods below cause hives, itching of the lips or throat, or more severe symptoms? Y N [Circle each] avocado (guacamole), apple, pear, celery, carrot, hazelnut, kiwi, papaya, pineapple, peach, cherry, plum, apricot, banana, melon, chestnut, fig, passion fruit, mango, raw tomatoes, or potatoes (problems after eating or peeling). II. Contact dermatitis assessment (for patients who wear latex gloves frequently): 1. Do you have a history of eczema or other rashes involving your hands? Y N 2. Do you have rash, or itching, cracking, ?chapping,? scaling, or weeping skin from latex glove use? Y N 3. Have these symptoms recently changed or worsened? Y N 4. Do you have these same or similar symptoms with nonlatex gloves or after stopping glove use? Y N III. Contact urticaria assessment (for patients who wear latex gloves frequently): When you wear or are around others wearing latex gloves, do you get hives; red, itchy, swollen hands within 30 minutes; or ?water blisters? on your hands within a day? Y N IV. Aerosol reaction assessment: 1. When you wear or are around others wearing latex gloves, have you noted any: A. Itchy, red eyes; fits of sneezing; runny or stuffy nose; or itching of the nose or palate? Y N B. Shortness of breath, wheezing, chest tightness, or difficulty in breathing? Y N C. Other acute reactions, including generalized or severe swelling or shock? Y N V. Miscellaneous reaction assessment: 1. Do you have a history of anaphylaxis or shock occurring during a surgical operation? Y N 2. Have you had itching, swelling, or other symptoms following dental, rectal, or pelvic examinations? Y N 3. Have you experienced swelling or difficulty in breathing after blowing up a balloon? Y N 4. Do condoms, diaphragms, or latex sexual aids cause itching or swelling? Y N 5. Do you have problems with plastic adhesive bandages? Y N

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