

Latex Allergy

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ABSTRACT

Allergy to natural rubber latex is an important clinical condition that occurred after the institution of universal precautions to protect healthcare workers. A rapid increase and production of both examination and surgical gloves resulted in an epidemic of allergy to latex protein. Healthcare workers in both the medical and dental environments, as well as specific groups of individuals including those with spina bifida, myelodysplasia, and food allergies (banana, kiwi, avocado, and others), were at increased risk of sensitization. Clinical symptoms in the latex allergic individual ranged from type I hypersensitivity reaction including rhinoconjunctivitis, asthma, and systemic reaction to type IV hypersensitivity reaction,

which occur from the chemicals added during the manufacturing process. Diagnosis of latex allergy is based on a clinical history that correlates the development of symptoms in relationship to exposure. In the United States there are no skin tests approved by the Food and Drug Administration. Therefore a combination of clinical judgment and serologic testing such as ImmunoCAP and Immulite is helpful. The primary treatment of latex allergy is avoidance of exposure to the latex protein. *Mt Sinai J Med* 78:759–772, 2011. © 2011 Mount Sinai School of Medicine

Key Words: latex allergy, latex sensitivity, natural rubber latex.

Allergy to natural rubber latex (NRL) gloves was identified as a serious health problem in the late 1980s and 1990s. The prevalence of latex allergy has been highest in certain groups, including healthcare workers (HCW), rubber industry workers, patients who have had multiple surgeries, and children with bladder extrophy or myelodysplasia. Allergy to NRL results through direct contact of skin, mucous membranes, and the respiratory tract with the allergens.

In the United States in recent years, the incidence of latex allergy has decreased significantly; however,

The prevalence of latex allergy has been highest in certain groups, including healthcare workers, rubber industry workers, patients who have had multiple surgeries, and children with bladder extrophy or myelodysplasia. It is estimated that >15 million people suffer from latex allergy worldwide. In the United States, 150,000 to 1 million healthcare workers suffer from latex allergy.

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worldwide the problem persists due to continued use of powdered latex gloves. It is estimated that >15 million people suffer from latex allergy worldwide. In the United States, 150,000 to 1 million HCW suffer from latex allergy.¹⁻³

The reform designed to provide maximum protection to HCW against blood-borne pathogens has unknowingly resulted in a debilitating occupational illness.⁴

HISTORICAL BACKGROUND

Archeologists have found that latex items were used as early as 1600 BC. The oldest rubber artifacts are from the El Manatí archeological site in Veracruz, Mexico. These artifacts consisted of rubber balls of various diameters documented by radiocarbon dating to be from 1600 BC. Additional artifacts from other sites in Mesoamerica include wooden tool handles wrapped with rubber, human figurines, and a stone tool hafted with a rubber band.⁵ In Central America, many Mayan ceremonial sites contained stone courts for playing a game with rubber balls, which supports the widespread ability to process latex into useful rubber balls. It was not until AD 1900 that surgical gloves were commonly used.⁶

MANUFACTURE OF NATURAL RUBBER LATEX

Ninety-nine percent of all commercial NRL comes from commercially grown *Hevea brasiliensis* trees, grown in a number of tropical countries including Malaysia, Thailand, and India. Smaller plants are located in Central and South America. The guayule bush (*Parthenium argentatum*) is another commercial source of latex. Proteins of the guayule do not appear to cross-react with *Hevea brasiliensis*.⁷

The milky-white sap of the commercially grown rubber tree *Hevea brasiliensis* is tapped from its bark and collected in small bowls. The functional unit of latex rubber is a spherical droplet (CIS-1, 4-polyisoprene) containing an outer layer of protein, lipid, and phospholipid that provides structural integrity. In addition, latex sap contains carbohydrates and other organic and inorganic constituents. There are >200 proteins in latex sap, but only Hev b1 through Hev b14 are known to be allergenic. Ammonia sometimes combined with thiurams is added to the collection bowls when the bark of the tree is tapped. This helps to prevent coagulation and bacterial contamination of the sap. This latex concentrate, the starting material

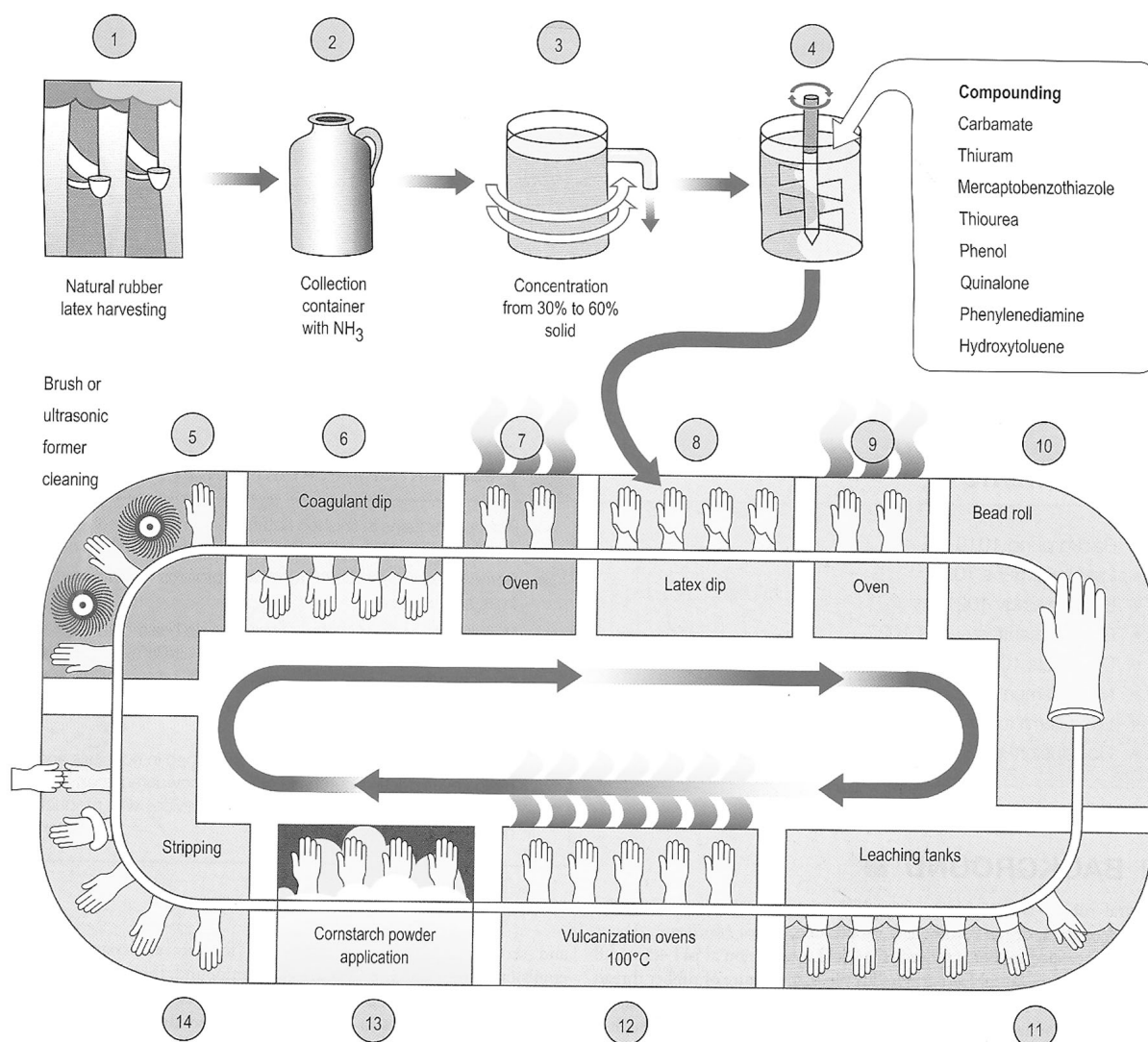
for NRL products, is mixed with as many as 200 compounding chemicals before being processed into various products. The latex is then converted into 2 types of raw materials, a liquid latex concentrate or solid dry rubber.⁸

The liquid latex concentrate plus compounding chemicals are processed into catheters, baby pacifiers, balloons, dental dams, gloves, or condoms. Glove-shaped porcelain formers pretreated with a coagulant are dipped into compounded latex, resulting in a deposition of a thin film of latex. Products are washed to remove excess chemicals and vulcanized at 100°C–120°C. Once vulcanization is complete, leaching is done again, then the item is dipped in a slurry tank where cornstarch powder is applied to the gloves before they are stripped from the former and packaged.⁹ After being dried and rinsed to reduce proteins and impurities, the gloves are dry-lubricated with cornstarch or talc powder. Powder particles adsorb residual latex proteins. If powder-free gloves are desired, the final step is a chlorination bath in lieu of a cornstarch bath¹⁰ (Figure 1).

Raw dry rubber is produced differently. Natural rubber latex is coagulated, creped, crumbled, washed extensively, then dried at >100°C. It is sold in solid bales and sheets. It is mixed with various chemicals as well as black carbon fillers, as is the case with automotive tires. It is found in footwear, engineering parts, adhesives, household articles, hoses, and tubing.

LATEX ALLERGENS

The development of latex allergy is dependent on sensitization to latex protein. A NRL standard preparation was assigned an arbitrary content of 100,000 allergen units (AU). In relation to this standard, the NRL allergen level was considered low at <10 au/mL, moderate at 10–100 AU/mL, and high at >100 au/mL. The range and amount of latex protein allergen content on latex gloves is dependent on brand, varying from 22 to 12,000 AU/mL of allergen, and can vary between gloves in the same batch.¹¹ Latex allergy is due to latex protein and it can result in a type 1 immunoglobulin E (IgE)-mediated hypersensitivity reaction. The chemicals mixed with the latex protein such as thiurams, mercapto benzothiazoles (MBT), and thiocarbonates are responsible for the type IV delayed hypersensitivity reaction. The latex allergen content of gloves is dependent on washing time during the manufacturing process. The risk of sensitization is also dependent on the amount of airborne allergen. Cornstarch powder increases the risk of sensitization as gloves are



Natural rubber glove manufacturing process; the steps shown may vary somewhat from one manufacturer to another. (Adapted from Hamann CP AmJ Contact Dermat 1993; 4:4.)

Fig 1. Manual rubber glove manufacturing process. **Abbreviations:** NH_3 , ammonia.

donned and removed; latex protein adherent to cornstarch particles becomes airborne and available for inhalation.^{12,13} Respirable latex particles can also be shed from powder-free gloves.¹⁴

Individuals at risk may be sensitized by the following mechanisms: inhalation of airborne latex, contact with mucosal surfaces, and/or contact with the skin when there are open lesions such as cuts or abrasions. Patients may be exposed during surgery through either intraperitoneal contact, intravenous infusion, or nasal tracheal intubation. Individuals may be sensitized by merely inhaling latex particles intranasally. There are certain high-risk situations for development of latex allergy (Table 1).^{11,15-19} These include medical and dental HCW and patients with repeated surgical procedures.²⁰

There are currently 14 accepted allergens. Hev b 1, 2, 3, 4, 5, 6, 6.01, 6.02, 7.01, 13, and 14 have been identified as the most sensitizing of the *Hevea* allergens. Disagreement exists as to the relevant importance of Hev b 2, Hev b 13 and Hev b 14. Management of latex allergic patients involves avoidance of all relevant latex allergens.²¹⁻²⁶

Hev b 1, also called the rubber elongation factor, is a major allergen in 80% of patients with spina bifida.^{21,27} Hev b 2 (b-1,3-gluconase) cross-reacts with a homologous protein in bell peppers.^{28,29} This suggests a connection to the latex food allergy syndrome. Hev b 3 is a small rubber particle. It shows strong IgE binding activity from patients with latex allergy and spina bifida. Hev b 4 IgE binding occurs in 65% of HCW and 97% of patients with spina bifida

Table 1. *Groups at Risk for Anaphylaxis to Latex.*^{15–20}

Groups at Risk	Prevalence of Latex Sensitization (%)
Spina bifida and congenital genitourinary abnormalities	18–73
Healthcare workers (housekeepers, laboratory workers, dentists, nurses, physicians)	3–17
Rubber industry workers	11
Atopic individuals (asthma, rhinitis, eczema)	6.8
Patients who have undergone multiple surgical procedures	6–50

and latex allergy, but is of minor importance in latex allergy. Hev b 5 is a major latex allergen in both HCW and patients with spina bifida. It is also a major allergen in diagnosis of latex allergy.²⁹ Hev b 6.01 is prohevein. It has demonstrated reactivity with IgE from sera of HCW and patients with spina bifida. Wagner and Breitender have documented the cross-reactivity of Hev b 6.02 (mature hevein) with fruits such as avocado and banana.²⁹ Hev b 6.02 has shown sequenced identity of >50% of class 1 chitinase in fruits.³⁰ Hev b 6.01 and Hev b 6.02 and Hev b 5 have been identified as major allergens for adults.²³ Hev b 7 Patatin homologue (Hev b 7.01/7.02) has cross-reactivity between potato and tomato. Hev b 8 (*Hevea* profilin) has cross-reactivity with banana, celery, birch and grass pollen, pineapple, and bell pepper.²⁹ Hev b 9 (*Hevea* enolase) is not an important allergen in HCW and spina bifida patients. Hev b 10 (manganese superoxide dismutase) has a low prevalence in allergic patients. Hev b 11 (class 1 chitinase) is

associated with the latex-fruit syndrome. Hev b 12 (lipid transfer protein) and Hev b 13 (esterase) do not play an important role (Table 2).²⁶ In a recent article, Lee stated that Hev b 14 is a major allergen in latex gloves in Taiwan. It is listed in World Health Organization and International Union of Immunological Societies nomenclature as a new latex allergen.^{23–25}

EPIDEMIOLOGY

The prevalence of latex allergy depends on the population studied, ranging from 3% to 64%. In the general population, the range is between 5% and 10%. Ownby *et al.* measured specific latex IgE antibody in 1000 volunteer blood donors and 996 ambulatory surgical patients. The rate of sensitization to NRL was 6.5% and 6.7%, respectively, but not clinically symptomatic.^{1,31}

Approximately 10% to 17% of HCW are sensitized and >2% have occupational asthma due to latex.³² In 1991, the US Food and Drug Administration (FDA) recalled latex barium enema tips after 16 deaths occurred in association with their use.³³ Others at risk for latex allergy are individuals who have cumulatively prolonged exposure to latex. Patients with spina bifida or urogenital abnormalities who have undergone repeated surgeries early in life may have prevalence of latex allergy >60%. This was noted in children with congenital urogenital anomalies requiring frequent catheterization and those who underwent multiple invasive surgeries involving mucosal contact with latex gloves. An epidemic of anaphylaxis in 7% of surgical procedures at Milwaukee Children's Hospital in the late 1980s

Table 2. *Hevea brasiliensis Latex Allergens.*²⁶

Name	Description	MW (kD)	Crossreactivity
Hev b 1*	Rubber elongation factor	58/14.6	Papain, fig
Hev b 2	Beta 1/3 glucanase	34–36	-
Hev b 3*	Prenyltransferase	24–27	-
Hev b 4	Microhelix	110/115	-
Hev b 5*	Acidic protein	16	Kiwi
Hev b 6.01	Hevein preprotein (prohevein)	20	Avocado, banana, chestnut
Hev b 6.02*	Hevein protein (mature hevein)	4.7	Avocado, banana, chestnut
Hev b 6.03	Hevein C-terminal fragment	15.3	Avocado, banana, chestnut
Hev b 7	Patatin homologue (Hev b 7.01/7.02)	43–46	Potato (patatin-Sol t 1)
Hev b 8	<i>Hevea</i> profilin	14–14.2	Pollens, celery
Hev b 9	<i>Hevea</i> enolase	51	Molds
Hev b 10	Mn superoxide dismutase	22–26	Molds
Hev b 11	Class I chitinase	33	Banana, avocado
Hev b 12	Lipid transfer protein	9.4	Peach and other stone fruit
Hev b 13	Esterase	42	-
Hev b 14	Hevamine	30	-

* "Indicator" proteins useful for assessment of the allergen content of rubber products or as markers of environmental exposure.

led to the identification of latex as the cause in this group of patients. Workers in the latex manufacturing industry are also at risk; there are reports of significant sensitization in latex doll manufacturing and a 3.7% prevalence in the glove industry.^{5,34,35}

In the 1980s and 1990s it was not unusual for HCW to use multiple powder gloves during a work shift. This was especially true in operating rooms, intensive care units, and labor and delivery suites. Healthcare workers would “snap” off their gloves and aerosolize the protein-laden powder into the environment. This “deadly dust” would produce significant symptoms in sensitized individuals and act as the stimulus to sensitize others.^{36,37}

Sampathi noted that the most common route for exposure to latex epitopes in the perioperative period in children is through mucosal and peritoneal surfaces from surgeons wearing latex gloves during intracavity exposure. This route of sensitization through mucosal surfaces could be responsible for anaphylactic reactions that occur in women during gynecological and obstetrical procedures.³⁸ Obstetrical and gynecological procedures account for 50% of all reactions caused by NRL. A higher incidence of latex sensitization has been reported

Obstetrical and gynecological procedures account for 50% of all reactions caused by natural rubber latex.

in pregnant patients. The female population also has a greater risk of sensitization due to repeated mucosal-surface exposure during obstetrical and gynecological procedures.^{39–41}

The fact that latex proteins are water soluble means they are easily eluted on mucous membranes, especially during exposure with multiple surgical procedures, removal of impactions, contact with mucous membranes and peritoneal surfaces, and inhalation of the allergen.^{37,42,43} Skin breakdown and abrasion is another source of exposure and sensitization. In addition, as already stated, individuals with spina bifida or urogenital abnormalities requiring multiple urinary tract catheterizations and multiple surgical procedures early in life were at increased risk.

The latex burden in gloves can be reduced by washing and chlorination. Currently, low protein, powder-free gloves have minimal potential to sensitize those not yet sensitized to latex. In countries where avoidance to latex has been promoted, the incidence of sensitization has decreased to 1%. However, worldwide, powdered latex gloves continue to be used, especially in underdeveloped

countries.⁴⁴ The institution of universal precautions in 1987 by the US Centers for Disease Control and Prevention resulted in an increased demand for NRL gloves. By 1987, universal precautions had

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been codified to include blood, semen, vaginal secretions, and various bodily fluids (cerebrospinal, amniotic, pericardial, peritoneal, and synovial).⁴⁵ The requirement caused latex glove production to increase from 800 million to 20 billion per year.^{4,46,47} A commonly held theory about the sudden increase in latex allergy is that this increased demand resulted in a decline in the quality of NRL gloves. The decline in quality is attributed to either established manufacturers cutting corners or the development of new companies with lesser manufacturing skills. It is assumed that this increased the latex protein content of NRL gloves. It is assumed that the agricultural techniques used to stimulate younger trees to produce a higher yield of latex per tree contributed to an increase in proteins in the NRL. In addition, the shorter storage times of latex sap resulted in less denaturing of the latex proteins, perhaps increasing the antigenicity. The prolonged storage of latex sap that had been typical in the past resulted in denaturing of the latex proteins. These factors, plus less washing during production, were felt to contribute to the epidemic of latex allergy.⁵

Swanson noted that aerosol dispersal of airborne latex clinging to cornstarch powder in gloves settles on work surfaces and clothing and becomes

Sensitization can occur through several means of exposure, including inhalation, mucous-membrane contact, peritoneal surfaces, abraded skin, and intravenous administration of drugs through latex ports.

a secondary source of exposure.³⁷ Therefore, sensitization can occur through several means of exposure, including inhalation, mucous-membrane contact, peritoneal surfaces, abraded skin, and intravenous administration of drugs through latex ports. During the last 25 years, scientific experimental and clinical studies have documented the dangers of cornstarch powder on examination and surgical

Table 3. *Cross-Reactive Foods.*

High risk	Avocado	Banana	Chestnut	Kiwi			
Moderate risk	Apple	Carrot	Celery	Melons	Papaya	Potato	Tomato
Low/undetermined risk	Apricot	Cherry	Citrus fruits	Fig	Grapes	Lychee	Mango
	Nectarine	Passion fruit	Peach	Pear	Persimmon	Pineapple	Strawberry
	Buckwheat	Rye	Wheat	Coconut	Hazelnut	Walnut	Castor bean
	Chickpea	Peanut	Soybean	Dill	Oregano	Sage	Peppers (cayenne, sweet, bell)
	Shellfish	Sunflower seeds					

gloves because the cornstarch promotes wound infection, causes serious peritoneal adhesions and granulomatous peritonitis, and is a well-documented vector of the latex allergy epidemic in the world.^{13,47}

The prevalence of IgE allergy to latex occurs with a greater prevalence in individuals who are atopic and have specific food allergies such as avocado, banana, kiwi, and chestnut. Turjanmaa noted that 50% of individuals who are allergic to NRL have food allergies. Other investigators have suggested that the incidence is as high as 50%–80%, but this depends on how food allergy is defined. If food allergy is defined by the presence of IgE antibody without clinical symptoms, then the percentage increases. Additional foods that have been implicated in latex-allergic individuals are apple, beet, buckwheat, wheat, flour, carrot, citrus fruit, fig, grapefruit, hazelnut, lettuce, peach, peanut, pear, spinach, strawberry, sweet pepper, tomato, watermelon, walnut, passion fruit, papaya, and pineapple (Table 3). These foods contain epitopes found in NRL. An individual who is allergic to NRL can have symptoms ranging from anaphylactic shock to worsening of asthma, eczema, oral facial swelling, and/or itching of eyes, ears, nose, and throat upon ingestion.¹⁰

Tarlo *et al.* reported in a study that by year 2 of clinical practice, 10% of 131 dental students and practitioners had positive skin prick test to NRL. Positive responses were seen from the second year of their clinical practice.⁴⁸ Additional reports have showed that sensitization could be prevented in dental students by the use of low-protein, powder-free gloves.⁴⁹

NONALLERGIC AND ALLERGIC CLINICAL MANIFESTATION

There are 4 possible types of reactions to NRL gloves: (1) irritant contact dermatitis, (2) allergic contact urticaria, (3) allergic contact dermatitis, and (4) anaphylaxis. The clinical manifestations of latex allergy are dependent on the route of exposure. The underlying mechanism is either non-IgE or

Table 4. *Types of Glove-Associated Reactions.*^{10,28}

Irritation	Irritant Contact Dermatitis
Type IV hypersensitivity	Delayed-type hypersensitivity; allergic contact dermatitis
Type I hypersensitivity	Immediate type hypersensitivity, occupational rhinitis, urticaria, occupational asthma, anaphylaxis

IgE-mediated. Irritant dermatitis is the most common form of nonallergic non-IgE-mediated dermatitis. The least common but potentially most serious reactions are due to type 1 IgE hypersensitivity. Examples range from contact urticaria, rhinoconjunctivitis, asthma, angioedema, and pharyngeal edema to a systemic reaction such as anaphylaxis (Table 4).

Irritant Contact Dermatitis

Irritant contact dermatitis is a non-IgE-mediated eczematous reaction caused by heat and friction under gloves. This is not an allergic reaction; it is due to direct injury of the epidermal cells or by destruction or removal of the protective intracellular lipids within minutes to hours after putting on gloves.⁵⁰ The severity of the reaction depends on the duration of exposure, degree of skin occlusion, and skin temperature. The irritant effects are the result of repeated hand-washing, use of detergents and sanitizers that are improperly rinsed off, or the application of cornstarch-powder gloves. Gloves enhance the effect by providing a warm, moist, occlusive environment allowing penetration of irritants. The cornstarch powder acts as an abrasive. The first symptoms are generally erythema, edema associated with pruritus, or burning occurring within minutes to hours. If exposure persists, then the skin becomes dry, thickened, cracked, fissured, and crusted with plaques and papules. Symptoms do not occur beyond the gloved area. The use of cotton-liner gloves may be helpful to prevent the problem.

Both synthetic and latex gloves can cause irritation due to chemicals, poor leaching, excessive use of biocides, or insufficient processing.⁵⁰

Allergic Contact Urticaria

Approximately 60%–80% of HCW who are sensitized to latex report contact urticaria of the hands. It is the most common early manifestation of latex allergy. Symptoms occur within 10 to 15 minutes after gloves are donned. This type 1 IgE-mediated reaction caused by NRL is frequently misdiagnosed as an irritant from hand-washing or glove powder. Sites remote to the hand that have been touched by the latex protein can also develop urticaria.⁴⁶ This can predate more profound allergic reaction.

Rhinitis, Conjunctivitis, and Asthma

Rhinitis, conjunctivitis, and asthma can occur in latex-sensitive individuals secondary to inhalation of cornstarch particles laden with latex being dispersed when gloves are put on and removed. Symptoms such as sneezing, ocular tearing and itching, and nasal congestion and rhinitis can occur, but are frequently confused with seasonal pollen allergies. It becomes critical to recognize the relationship of these symptoms to latex aero allergen exposure. Asthma can occur as an isolated entity in relation to latex exposure in individuals not previously diagnosed with asthma.¹⁰ These individuals will have respiratory symptoms such as chest tightness, wheeze, shortness of breath, dyspnea, and cough.

Occupationally exposed individuals who have latex-induced asthma need to be removed from the work environment unless exposure can be eliminated or sufficiently decreased. The resultant exposure may result in permanent airway damage similar to other occupational exposures.^{51–53}

Allergic Contact Dermatitis—Type IV Allergy

Contact dermatitis, a type IV delayed hypersensitivity reaction, occurs after wearing latex gloves.⁴⁶ The reaction is typically a response to the chemicals that are added during the manufacturing process and not to the NRL. The responsible allergens are thiurams, carbamates, MBT, and phenylendiamine. It is a T-cell-mediated reaction due to wearing rubber gloves, or handling sports equipment, shoes, or medical devices. The rash appears 24–48 hours after contact with the offending allergen. Repeated contact with the same allergen results in an itchy rash that usually starts with vesicles on the top of the hand and is eczematous. If exposure continues, the skin becomes dry, crusted, and lichenified. Resultant breaks in the skin barrier increase the risk of

sensitization to NRL. Skin lesions can extend beyond the gloved hand.⁹

Anaphylaxis

The most serious type 1 IgE hypersensitivity reaction to NRL is anaphylaxis. It can occur in both medical and nonmedical settings after the use of latex-based products. These events can occur intraoperatively during surgery, childbirth, gynecological and obstetrical procedures, and dental or other medical procedures. It therefore is important to identify the group of patients who are at risk; due to the life-threatening nature of this reaction, it must be immediately recognized.⁵⁴

Additionally, anaphylaxis can occur from contact with toy balloons, condoms, diaphragms, rubber-handled squash racquets, pacifiers, bottle nipples, adhesives for hair extensions, and padding in children's play pits. Symptoms may include airway obstruction, cardiovascular collapse, hypotension, or generalized angioedema. A balloon touching the lips and/or tongue of a latex-allergic individual can result in swelling of the lip and/or tongue.^{38,55}

DIAGNOSIS

The diagnosis of latex allergy is challenging. The most important aspect, as in other allergic conditions, is the clinical history. It is important to look for supporting associations between latex exposure and the development of symptoms. Swelling of the lip and/or tongue after a child has been playing with a toy latex balloon is frequently an early warning sign of latex allergy.³⁸

Latex sensitization has been reported more frequently in women. This may be due to more frequent exposure to NRL during working time and through greater mucosal contact with latex barrier contraceptives. Women are at a higher risk for latex allergy due to multiple gynecological and obstetrical procedures, most likely due to extensive contact of latex gloves with highly absorptive mucous membranes.^{39–41} Lieberman reports that latex accounts for 50% of the allergic reactions during obstetrical procedures, 20% during abdominal operations, and 10% during orthopedic procedures.⁵⁶

In obtaining a history, it is important to obtain a patient's individual history of atopy, including evidence of seasonal allergic rhinitis, eczema, asthma, and food allergy (banana, kiwi, avocado, and chestnut). A correlation between cross-reacting foods, fruits, and vegetables is frequently seen. In addition,

history of multiple surgeries and occupational exposures has to be explored. The frequency, the nature, the magnitude, and the duration of the patient's occupational exposure to NRL must be identified, as well as the symptoms that occur. A questionnaire can help facilitate the interview. The questionnaire from the American Latex Allergy Association is quite helpful (Figure 2). Once the clinical history is completed, the next step is to confirm IgE sensitivity to latex. This can be done serologically or by skin test. Bencard (Ontario, Canada) produces a commercially available extract with 93% sensitivity.³²

It is important in clinical history-taking to assess the patient's individual atopic history including evidence of seasonal allergic rhinitis, asthma, eczema and food allergy. Secondly, it is important to get information about the patient's occupational exposure to help identify repetitive use of rubber products. In addition the magnitude and nature of the exposure should be queried. The relationship to exposure and the type symptoms that occur help distinguish between individuals with type 1 and type IV reactions. In addition, multiple surgeries (ie, >5) with general anesthesia are all aids in determining a positive latex allergy history.^{31,54}

Skin testing is the most sensitive means of detecting IgE-mediated reactions. In Europe and Canada where commercial extracts are available, this is the procedure of choice. Skin prick tests are widely performed in Europe and Canada.³² The skin test procedures are performed with a lancet pricking the skin through a drop of latex extracts at sequential concentrations of 0.001–1 mg/mL of protein. The results are read after 15 minutes and are compared with a negative saline control and histamine.

In the United States there are no commercially available, FDA-approved skin test reagents for latex.^{57,58} This has forced many allergists to create a homemade extract from examination gloves soaked in diluent. This results in an unstable, uncharacterized product of variable potency. The lack of characterization of the hevea allergen in such products has resulted in false-negative results due to low allergen content or systemic reaction due to high levels of hevea allergen.^{3,59–61}

Provocation testing has been used by investigators. Specific nasal provocation and inhalation challenge tests are reliable but only available at a few research centers.⁶² This involves inhalation of the latex laden powder in a controlled environment. These are not suitable for routine clinical use and should stay in research settings. Provocation testing should be discouraged due to the risk of false-negative and anaphylactic response due to variability latex protein content from glove to glove.



Risk Factor Assessment: Circle Y or N

Exposure History:

Are you a health care worker?	Y	N
Do you wear latex gloves regularly or are you otherwise exposed to latex regularly?	Y	N
Do you have a history of eczema or other rashes on your hands?	Y	N
Do you have a medical history of frequent surgeries or invasive medical procedures?	Y	N
Did these take place when you were an infant?	Y	N
Do you have a history of "hay fever" or other common allergies?	Y	N
Do your fellow workers wear latex gloves regularly?	Y	N
Do you take a beta-blocker medication?	Y	N

Circle any foods below that cause hives, itching of the lips or throat, or more severe symptoms when you eat or handle them:

avocado	apple	pear	celery	carrot	hazelnut
kiwi	papaya	pineapple	peach	cherry	plum
apricot	banana	melon	chestnut	nectarine	grape
fig	passion fruit	tomatoes	potatoes		

Contact Dermatitis Assessment: (for patients who wear latex gloves frequently)

Do you have rash, itching, cracking, chapping, scaling, or weeping of the skin from latex glove use?	Y	N
Have these symptoms recently changed or worsened?	Y	N
Have you used different brands of latex gloves?	Y	N
If so, have your symptoms persisted:	Y	N
Have you used non-latex gloves?	Y	N
If so, have you had the same or similar symptoms as with latex gloves?	Y	N
Do these symptoms persist when you stop wearing all gloves?	Y	N

Contact Urticaria (Hives) 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 you hands within a day?	Y	N
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Aerosol Reaction Assessment:

When you wear or are around others wearing latex gloves, have you noted any:

Itchy, red eyes, fits of sneezing, runny or stuffy nose, itching of the nose or palate:	Y	N
Shortness of breath, wheezing, chest tightness or difficulty breathing?	Y	N
Other acute reactions, including generalized or severe swelling or shock	Y	N

History of Reactions Suggestive of Latex Allergy:

Do you have a history of anaphylaxis or of intra-operative shock?	Y	N
Have you had itching, swelling or other symptoms following dental, rectal or pelvic exams?	Y	N
Have you experienced swelling or difficulty breathing after blowing up a balloon?	Y	N
Do condoms, diaphragms or latex sexual aids cause itching or swelling?	Y	N
Do rubber handles, rubber bands or elastic bands or clothing cause any discomfort?	Y	N

Fig 2. American Latex Allergy Association Risk Factor Assessment.

The use test is another method to be discouraged. It involves placing a single digit in a glove finger for 20 minutes and observing the patient for development of pruritus, erythema, hives, or allergic symptoms.^{57,63} If no reaction occurs, then

a moistened hand is placed in an examination glove. A control vinyl glove may be placed on the opposing hand. Some investigators prick 3 sites on the glove and observe for a response in 20 minutes. The variation in latex protein can be considerable from glove to glove in the same batch.⁴⁷ These procedures are extremely hazardous and should be discouraged due to risk of systemic reactions.⁶⁴

Greer Laboratories has been doing research to develop an FDA-approved extract, but none is available to date. The problem revolves around the variety epitopes for latex allergy.^{65,66} Tom Grier, PhD, medical affairs officer at Greer Laboratories (Lenoir, NC), stated that the complexity of the clinical trials and variety of patients with latex allergy led to a discontinuation of the trials and product development of latex skin test materials by Greer (T. Grier, personal communication, June 29, 2011).

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In the United States, physicians must rely on clinical judgment, history, and serological testing in symptomatic patients as the method of choice in diagnosing latex allergy.

symptomatic patients as the method of choice in diagnosing latex allergy. Standard patch testing is done to determine contact allergens in those who have contact dermatitis.

In vitro testing is designed to measure IgE antibody in serum. It is a preferred alternative to skin prick testing when commercial extracts are not available. Two serologic methods are currently widely used throughout the world: ImmunoCAP (Phadia) and the Immulite autoanalyzer (Siemens). Human test serum is incubated with Hevea latex allergen containing reagent. The results are interpolated from a total IgE calibration curve in kU_A/L. ImmunoCAP and Immulite assay have a diagnostic sensitivity and specificity of approximately 80% and >95%, respectively, when compared with skin puncture. A negative blood test does not rule out latex allergy. At this time, a chip-based microarray containing 8 Hev b allergens is being developed. It has been shown to more clearly define the specificity of IgE anti-latex with no loss of diagnostic sensitivity.⁶⁷ Results from one study suggest that this can distinguish between patients with clinical sensitization and allergy.⁶⁸ A commercial test is under investigation.

In the United States, the diagnostic testing procedure of choice is ImmunoCAP or the Immulite. In other parts of the world, where characterized skin test reagents are available, skin test can be performed first. If the skin test data is inconsistent with the history, then one of the IgE antibody serology tests can be done.

PREVENTION AND MANAGEMENT

The primary means to prevent latex allergy is to avoid latex products from birth.³⁸ Once latex allergy develops, avoidance of latex products becomes essential. For patients who are allergic to the chemical additives and have developed contact dermatitis, avoidance of specific chemicals is important. Patients need to be patch-tested to determine which chemicals are causing the contact dermatitis and alternative products should be utilized that are free of these specific chemicals.

Patients with a history of systemic reaction to latex should wear a medical alert bracelet and carry an EpiPen (Dey Pharma) at all times for the treatment of anaphylaxis. In addition, they should carry nonlatex gloves to be used in settings where providers may not have them readily available. Ongoing exposure to latex by allergic individuals puts them at risk for increasing sensitivity and severity of allergic reactions.

In hospitals and medical or dental office settings, clear guidelines should be in place to manage the latex-allergic individuals. Latex-safe areas should be provided and are defined as those containing nonlatex materials. These include gloves, catheters, intravenous equipment, surgical tape, tourniquets, ventilation, airway equipment, and medication without latex stoppers. On hospital floors and in medical and dental offices, emergency carts should be available that have latex-free material.⁵⁶

It is difficult to make operating rooms totally latex free due to the fact that equipment may contain components made from latex. Ideally, patients in an environment where latex and or powder latex gloves are still used should be scheduled as the first case of the day in a room that has been carefully cleaned. Hospitalized patient rooms, beds, charts, and arm bracelets should be identified as latex allergic to avoid possible exposure.⁵⁶

The primary source of sensitization in the medical and dental environment are the NRL examination and surgical gloves, both sterile and nonsterile. The powdered version is the worst offender. Avoidance of this material is the best means of prevention.^{37,69}

Latex-allergic HCW should be provided with a latex-safe environment established by institutional guidelines that dictate a policy of latex glove use. It is not enough to provide allergic HCW with NRL-free gloves; coworkers must also be provided with alternative gloves. Environmental contamination with NRL continues to occur when HCW who are not allergic use their “special gloves,” putting the allergic individual at risk for both further sensitization and systemic reactions. In some cases, low-protein powder-free gloves may be used, but this does not guarantee a negative risk of reaction for the allergic HCW. According to Jean Bousquet in a recent meta-analysis, further studies are needed to evaluate whether low-powdered NRL is the preferred glove to use to prevent sensitization in HCWs.⁷⁰

Latex-allergic individuals need to be aware of the fact that there are >40,000 products that contain NRL. Hevea latex products used in the healthcare setting

Latex-allergic individuals need to be aware of the fact that there are >40,000 products that contain natural rubber latex. Hevea latex products used in the healthcare setting must be labeled as containing natural rubber latex with a black-box warning, according to the Food and Drug Administration. Such stringent labeling is not required on consumer products, and unwitting consumers may be inadvertently exposed to latex and have an adverse event

must be labeled as containing NRL with a black-box warning, according to the FDA. Such stringent labeling is not required on consumer products, and unwitting consumers may be inadvertently exposed to latex and have an adverse event (Tables 5 and 6). In environments where there is absolutely no risk of body-fluid contamination, NRL use should be discouraged. Food handlers, florists, beauticians, and toll-takers do not need to use NRL. They risk sensitizing themselves and accidentally exposing the latex-allergic individual. Food preparers can transfer latex protein to food that is handled and then potentially ingested by a latex-allergic patient (Table 7).

Table 5. *Natural Rubber Latex Products Found in a Medical Setting.**

Gloves (examination, surgical, household)	Tourniquets, blood pressure cuffs
Stethoscopes	Catheters
Intravenous tubing ports, syringe plungers	Electrode pads
Goggles	Respirators
Wound drains and tubes	Multidose vial tops
Dental dams	Tires
Handgrips	Carpet
Shoe soles	Elastic in clothing
Face masks	Adhesive tape
Mattresses on stretchers	Ambu bags
Bulb syringes	PCA syringes

*From American Latex Allergy Association (<http://latexallergyresources.org>).

Table 6. *Natural Rubber Latex Products Found in the Home.**

Bandages	Baby-bottle nipples
Balloons	Carpet backing
Condoms	Diaphragms
Douche bulbs	Elastic in clothing and disposable diapers
Erasers	Eye-dropper bulbs
Hot-water bottles	Rubber balls
Pacifiers, teethingers	Adhesives for hair extensions
Rubber hand grips on racquets, bicycles, garden tools	Rubber bands, dental coffer dams
Rubber clothing (raincoats)	Rubber gloves
Rubber toys	Shoes
Sports equipment	Sanitary and incontinence pads
Computer mouse pads	Buttons on electronic equipment

*From American Latex Allergy Association (<http://latexallergyresources.org>).

The use of pharmacotherapy to treat anaphylaxis, allergic contact dermatitis, and allergic rhinoconjunctivitis is helpful. In latex-allergic patients, pretreatment before exposure to latex has not been proven to be effective as it is in patients with

In latex allergic patients, pretreatment before exposure to latex has not been proven to be effective as it is in patients with radiographic contrast media allergy.

radiographic contrast media allergy.⁵⁶ Immunotherapy had been attempted using both oral and subcutaneous methods, with variable efficacy. At this

Table 7. *Occupations in Which Latex Gloves Are Commonly Used.*

Healthcare workers
Food handlers/restaurant workers
Domestic workers
Hairdressers
Security personnel
Construction workers
Greenhouse workers/gardeners
Florists
Funeral home workers
First responders (police officers, firefighters, ambulance attendants)
Rubber plantation workers

time there are no viable options; however, novel approaches to immunotherapy are under investigation and still in the experimental stages.^{71–73}

Patient education is critical. Patients must be aware of where NRL products may be found. They need to wear a medical alert bracelet that identifies them as being latex allergic. The latex-allergic individual should notify all HCW and dentists of their latex allergy. This information needs to be identified when surgery or any medical procedures are to be done so that they can be provided with a latex-safe environment. Nonlatex gloves should be carried by these individuals so they are prepared if a situation arises where the gloves are needed and not available. Educational materials for the latex-allergic individual can be obtained from the American Latex Allergy Association (<http://latexallergyresources.org>), American College of Allergy, Asthma and Immunology (<http://www.acaai.org>), and the American Academy of Allergy, Asthma and Immunology (<http://www.aaaai.org>).

A variety of synthetic elastomers are available for use in the healthcare setting. These include butyl rubber, petroleum-based products with no allergenic protein polymers of 2-chlorobutadiene (neoprene), and copolymers of butadiene and acrylonitrile.⁷²

In medical settings, the predominant nonsterile nonlatex examination gloves are nitril, neoprene, vinyl, or synthetic polyisoprene rubber. The ability to provide barrier protection and to be sterilized varies between products.

The future appears promising in that manufacturers are attempting to develop a latex-safe glove with appropriate barrier protection. One such glove, Vylex, an enhanced latex material with ultralow levels of antigenic protein, could eliminate the risk of developing allergies. This product is still under investigation in order to confirm the safety of this glove in individuals who are latex allergic. Yolex, another nonhevea product, made from the guayule plant, is considered safe in the latex allergic patient.^{7,74,75}

CONCLUSION

It has been my personal observation that, despite the widespread nature of latex allergy, there is still a paucity of knowledge among medical students, residents, and physicians. Despite the decrease in incidence, latex allergy has not gone away. Patients who are latex allergic are still unwittingly being exposed accidentally by HCW, food handlers, housekeepers, beauticians, and toll-takers who continue to use latex gloves inappropriately.

In conclusion, latex allergy continues to be a problem worldwide. Identification of patients through clinical history and appropriate diagnostic testing is critical to prevent further sensitization. Patient safety is primary. Patients must be educated about avoidance of latex and treatment of allergic reactions, and those at serious risk must carry self-injectable epinephrine pens. Ongoing research may provide us with safe alternative gloves and perhaps immunotherapy to be utilized on sensitized patients. Appropriate use of nonlatex examination and surgical gloves is critical to prevent new sensitization that can trigger the classic symptoms of latex allergy, which are rhinoconjunctivitis, sneezing, ocular itching, wheezing, occupational asthma, and anaphylaxis.

In countries that have switched to powder-free, low-allergen latex gloves, a decrease in latex allergy has been noted.^{76,77} To date, approximately 90% powder-free gloves are used in Germany, with a 50% decline in latex allergies noted within a period of 2 years. In France a similar situation occurred with withdrawal of latex gloves from a hospital in Montpellier. Allergy symptoms and sensitization were reduced. Similar reports have come from Scandinavia, Canada, and the United States, where certain hospitals have achieved removal of latex powdered gloves.

Realizing the dangers of cornstarch on examination and surgical gloves, Germany's regulations of personal protective equipment banned the use of surgical glove powder cornstarch in 1997. In 2000, the purchasing supply agency for the United Kingdom ceased to purchase any gloves lubricated with cornstarch. Realizing the dangers of cornstarch on medical gloves, many hospitals and clinics in the United States have banned the use of cornstarch powdered examination and surgical gloves. Hospitals that have banned cornstarch on their examination and surgical gloves have noted a marked reduction in the latex allergy epidemic in their facility. Edlich and 11 coauthors submitted a Citizen's Petition to the FDA to ban cornstarch on medical gloves on September 24, 2008. From February 5 through April 25, 2011, the FDA had

a site on the Federal Register to assess the dangers of cornstarch powder on medical gloves. An FDA committee is now meeting to make a final decision on banning cornstarch on medical gloves in the United States.^{76–82}

DISCLOSURES

Potential conflict of interest: Nothing to report.

REFERENCES

- Ownby DR, Ownby HE, McCullough J, et al. The prevalence of anti-latex IgE antibodies in 1000 volunteer blood donors. *J Allergy Clin Immunol* 1996; 97: 1188–1192.
- Merrett T, Merrett S, Kekwick R. Prevalence of latex specific IgE antibodies in the UK [abstract]. *Ann Allergy Asthma Immunol* 1995; 74: 50.
- Kelly KJ, Kurup VP, Reijula KE, et al. The diagnosis of natural rubber latex allergy. *J Allergy Clin Immunol* 1994; 93: 813–816.
- Sussman GL, Beezhold DH, Liss G. Latex allergy: historical perspective. *Methods* 2002; 27: 3–9.
- Hosler D, Burkett SL, Tarkanian MJ. Prehistoric polymers: rubber processing in ancient Mesoamerica. *Science* 1999; 284: 1988–1991.
- Ownby DR. A history of latex allergy. *J Allergy Clin Immunol* 2002; 110(2 suppl): S27–S32.
- Siler DJ, Cornish K, Hamilton RG. Absence of cross reactivity of IgE antibodies from subjects allergic to *Hevea brasiliensis* latex with a new source of natural rubber latex allergy from guayule (*Parthenium argentatum*). *J Allergy Clin Immunol* 1996; 98(5 part 1): 895–902.
- Yip E, Cacioli P. The manufacture of gloves from natural rubber latex. *J Allergy Clin Immunol* 2002; 110(2 suppl): S3–S14.
- Hamann CP. Natural rubber latex protein sensitivity in review. *Am J Contact Dermat* 1993; 4: 4–21.
- Yunginger JW. Natural rubber latex allergy. In: Middleton EF Jr, Ellis EF, Yunginger JW, et al., eds. *Middleton's Allergy: Principles and Practice*. 7th ed. Vol. 2. St. Louis, MO: Mosby; 1998:1019–1020.
- Palosuo T, Mäkinen-Kiljunen S, Alenius H, et al. Measurement of natural rubber latex allergen levels in medical gloves by allergy specific IgE-ELISA inhibition, RAST inhibition and skin prick test. *Allergy* 1998; 53: 59–67.
- Brehler R, Kolling R, Webb M, et al. Glove powder—a risk factor for the development of latex allergy. *Eur J Surg Suppl* 1997; 579: 23–25.
- Edlich RF, Long WB III, Gubler DK, et al. Dangers of cornstarch powder on medical gloves: seeking a solution. *Ann Plast Surg* 2009; 63: 111–115.
- Phillips ML, Meagher CC, Johnson DL. What is “powder-free”? Characterisation of powder aerosol produced during simulated use of powdered and powder-free latex gloves. *Occup Environ Med* 2001; 58: 479–481.
- Slater JE, Mostello LA, Shaer C. Rubber-specific IgE in children with spina bifida. *J Urol* 1991; 146(2 part 2): 578–579.
- Shield SW, Blaiss MS. Prevalence of latex sensitivity in children evaluated for inhalant allergy. *Allergy Proc* 1992; 13: 129–131.
- Sussman GL, Lem D, Liss G, et al. Latex allergy in housekeeping personnel. *Ann Allergy Asthma Immunol* 1995; 74: 415–418.
- Lagier F, Vervloet D, Lhermet I, et al. Prevalence of latex allergy in operating room nurses. *J Allergy Clin Immunol* 1993; 90(3 part 1): 319–322.
- Moneret-Vautrin DA, Beaudouin E, Widmer S, et al. Prospective study of risk factors in natural rubber latex hypersensitivity. *J Allergy Clin Immunol* 1993; 92: 668–677.
- Arrellano R, Bradley J, Sussman G. Prevalence of latex sensitization among hospital physicians occupationally exposed to latex gloves. *Anesthesiology* 1992; 77: 905–908.
- Sussman GL, Beezhold DH, Kurup VP. Allergens and natural rubber proteins. *J Allergy Clin Immunol* 2002; 110(2 suppl): S33–S39.
- Palosuo T, Lehto M, Kotovuori A, et al. Latex allergy: low prevalence of immunoglobulin E to highly purified proteins Hev b 2 and Hev b 13. *Clin Exp Allergy* 2007; 37: 1502–1511.
- Lee MF, Chen YH, Lin HC, et al. Identification of heveamine and heve B 1 as major latex allergens in Taiwan. *Int Arch Allergy Immunol* 2006; 139: 38–44.
- Lee MF, Wang NM, Han JL, et al. Estimating allergenicity of latex gloves using Hev b 1 and Heveamine. *J Investig Allergol Clin Immunol* 2010; 20: 499–505.
- Yeang HY. Natural rubber latex allergens: new developments. *Curr Opin Allergy Clin Immunol* 2004; 4: 99–104.
- Hamilton RG. Latex allergy: epidemiology, clinical manifestations, and diagnosis. <http://www.uptodate.com/contents/latex-allergy-epidemiology-clinical-manifestations-and-diagnosis>. Updated February 18, 2011. Accessed May 30, 2011.
- Chen Z, Cremer R, Posch A, et al. On the allergenicity of Hev b 1 among health care workers and patients with spina bifida allergic to natural rubber latex. *J Allergy Clin Immunol* 1997; 100: 684–693.
- Risenga SM. Latex allergy revisited: a review. *Curr Allergy Clin Immunol* 2010; 23: 4–7.
- Wagner S, Breiteneder H. Hevea brasiliensis latex allergens: current panel and clinical relevance. *Int Arch Allergy Immunol* 2005; 136: 90–97.
- Kurup VP, Yeang HY, Sussman GL, et al. Detection of immunoglobulin antibodies in the sera of patients with purified latex allergens. *Clin Exp Allergy* 2000; 30: 359–369.
- Lebenbom-Mansour MH, Oesterle JR, Ownby DR, et al. The incidence of latex sensitivity in ambulatory surgical patients: a correlation of historical factors with positive serum immunoglobulin E levels. *Anesth Analg* 1997; 85: 44–49.
- Turjanmaa K. Incidence of immediate allergy to latex gloves in hospital personnel. *Contact Dermatitis* 1987; 17: 270–275.
- Gelfand DW. Barium enemas, latex balloons and anaphylactic reactions. *Am J Roentgenol* 1991; 156: 1–2.

34. Tarlo SM, Wong L, Roos J, et al. Occupational asthma caused by latex in surgical glove manufacturing plant. *J Allergy Clin Immunol* 1990; 85: 626–631.
35. Orfan NA, Reed R, Dykewicz MS, et al. Occupational asthma in a latex doll manufacturing plant. *J Allergy Clin Immunol* 1994; 94: 826–830.
36. Alenius H, Mäkinen-Kiljunen S, Turjanmaa K, et al. Allergen and protein content of latex gloves. *Ann Allergy* 1994; 73: 315–320.
37. Swanson MC, Bubak ME, Hunt LW, et al. Quantification of occupational latex aeroallergens in a medical center. *J Allergy Clin Immunol* 1994; 94(3 part 1): 445–451.
38. Sampathi V, Lerman J. Case scenario: perioperative latex allergy in children [published correction appears in *Anesthesiology* 2011; 114: 1258]. *Anesthesiology* 2011; 114: 673–680.
39. Draisci G, Zanfini B, Nucera E, et al. Latex sensitization a special risk for the obstetric population? *Anesthesiology* 2011; 114: 565–569.
40. Draisci G, Nucera E, Pollastrini E, et al. Anaphylactic reactions during cesarean section. *Int J Obstet Anesth* 2007; 16: 63–67.
41. Santos R, Hernández-Ayup S, Galache P, et al. Severe latex allergy after a vaginal examination during labor: a case report. *Am J Obstet Gynecol* 1997; 177: 1543–1544.
42. Carillo T, Cuevas M, Muñoz M, et al. Contact urticaria and rhinitis from latex surgical gloves. *Contact Dermatitis* 1986; 15: 69–72.
43. Turjanmaa K, Reunala T, Alenius H, et al. Allergens in latex surgical gloves and glove powder [letter]. *Lancet* 1990; 336: 1588.
44. Global rubber gloves market: an analysis. 2009. <http://www.aarkstore.com/reports/Global-Rubber-Gloves-Market-An-Analysis-12679.html>. Accessed May 30, 2011.
45. Centers for Disease Control and Prevention. Recommendations for prevention of HIV transmission in health-care settings. *MMWR Morb Mortality Wkly Rep* 1987; 36(suppl): 35–185.
46. Hunt LW, Fransway AF, Reed CE, et al. An epidemic of occupational allergy to latex involving health care workers. *J Occup Environ Med* 1995; 37: 1204–1209.
47. Edlich RF. *Medicine's Deadly Dust: A Surgeon's Wake-up Call to Society*. St. Petersburg, FL: Vandamere Press; 1997.
48. Tarlo SM, Sussman GL, Holness DL. Latex sensitivity in dental students and staff: a cross sectional study. *J Allergy Clin Immunol* 1997; 99: 396–401.
49. Levy DA, Allouache S, Chabane MH, et al. Powder-free protein-poor natural rubber latex gloves and latex sensitization [letter]. *JAMA* 1999; 281: 988.
50. Heese A, van Hintzenstern J, Peters KP, et al. Allergic and irritant reactions to rubber gloves in medical health services: spectrum, diagnostic approach, and therapy [published correction appears in *J Am Acad Dermatol* 1992; 26(3 part 2): 403]. *J Am Acad Dermatol* 1991; 25(5 part 1): 831–839.
51. LaMontagne AD, Radi S, Elder DS, et al. Primary prevention of latex-related sensitization in occupational asthma: a systematic review. *Occup Environ Med* 2006; 63: 359–364.
52. Liss GM, Tarlo SM. Natural rubber latex-related asthma: association with interventions and glove changes over time. *Am J Ind Med* 2001; 40: 347–353.
53. Tarlo SM, Wong L, Roos J, et al. Occupational asthma caused by latex in a surgical glove manufacturing plant. *J Allergy Clin Immunol* 1990; 35: 626–631.
54. Kelly KJ, Pearson ML, Kurup VP, 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.
55. Cogen FC, Beezhold DH. Hair glue anaphylaxis: a hidden latex allergy. *Ann Allergy Asthma Immunol* 2002; 88: 61–63.
56. Lieberman P. Anaphylactic reactions during surgical and medical procedures. *J Allergy Clin Immunol* 2002; 110(2 suppl): S64–S69.
57. Hamilton RG, Adkinson NF Jr. Validation of the latex glove provocation procedure in latex-allergic subjects. *Ann Allergy Asthma Immunol* 1997; 79: 266–272.
58. Turjanmaa K, Alenius H, Mäkinen-Kiljunen S, et al. Commercial skin prick test preparations in the diagnosis of rubber latex allergy [abstract]. *J Allergy Clin Immunol* 1994; 93: 299.
59. Yunginger JW, Jones RT, Fransway AF, et al. Extractable latex allergens and proteins in disposable medical gloves and other rubber products. *J Allergy Clin Immunol* 1994; 93: 836–842.
60. Kujala V, Alenius H, Palosuo T, et al. Extractable latex allergens in airborne glove powder and in cut glove pieces. *Clin Exp Allergy* 2002; 32: 1077–1081.
61. Yeang HY, Hamilton RG, Berstein DI, et al. Allergen concentration in natural rubber latex [published correction appears in *Clin Exp Allergy* 2010; 40: 831]. *Clin Exp Allergy* 2006; 36: 1078–1086.
62. Charous BL, Tarlo SM, Charous MA, et al. Natural rubber latex allergy in the occupational setting. *Methods* 2002; 27: 15–21.
63. Kelly KJ, Kurup V, Zacharisen M, et al. Skin and serologic testing in the diagnosis of latex allergy. *J Allergy Clin Immunol* 1993; 91: 1140–1145.
64. Jaeger D, Kleinhans D, Czuppon AB, et al. Latex-specific proteins causing immediate type cutaneous, nasal, bronchial and systemic reactions. *J Allergy Clin Immunol* 1992; 89: 759–768.
65. Hamilton RG, Adkinson NF Jr. Natural rubber latex skin testing reagents: safety and diagnostic accuracy of nonammoniated latex, ammoniated latex, and latex rubber glove extracts. *J Allergy Clin Immunol* 1996; 98(5 part 1): 872–883.
66. Hamilton RG, Biagini RE, Krieg EF. Diagnostic performance of Food and Drug Administration-cleared serologic assays of natural rubber latex-specific IgE antibody. The Multi-Center Latex Skin Testing Study Task Force. *J Allergy Clin Immunol* 1999; 103(5 part 1): 925–930.
67. Ott H, Schröder C, Raulf-Heimsoth M, et al. Microarrays of recombinant Hevea brasiliensis proteins: a novel tool for the component-resolved diagnosis of natural rubber latex allergy. *J Invest Allergol Clin Immunol* 2010; 20: 129–138.
68. Ebo DG, Hagendorens NM, DeKnop KJ, et al. Component-resolved diagnosis from latex allergy by microarray. *Clin Exp Allergy* 2010; 40: 348–358.
69. Heilman DK, Jones RT, Swanson MC, et al. A prospective controlled study showing that rubber gloves are the major contributor to latex aeroallergens in the operation room. *J Allergy Clin Immunol* 1996; 98: 325–330.

70. Bousquet J, Flahault A, Vandenplas O, et al. Natural rubber latex allergy among health care workers: a systematic review of the evidence. *J Allergy Clin Immunol* 2006; 118: 447–454.
71. Leynadier F, Herman D, Vervloet D, et al. Specific immunotherapy with a standardized latex extract versus placebo in allergenic healthcare workers. *J Allergy Clin Immunol* 2000; 106: 585–590.
72. Bernardini R, Campodonico P, Burastero S, et al. Sublingual immunotherapy with a latex extract in pediatric patients: a double-blind, placebo-controlled study. *Current Med Res Opin* 2006; 22: 1515–1522.
73. Rolland JM, Drew AC, O'Hehir RE. Advances in development of hypoallergenic latex immunotherapy. *Curr Opin Allergy Clin Immunol* 2005; 5: 544–551.
74. Renaud MY. Composition of synthetic latexes used for manufacturing gloved by the dipping process. *Clin Rev Allergy* 1993; 11: 363–370.
75. Carey AB, Cornish K, Schrank P, et al. Cross-reactivity of alternative plant sources of latex in subjects with systemic IgE-mediated sensitivity to *Hevea brasiliensis* latex. *Ann Allergy Asthma Immunol* 1995; 74: 317–320.
76. Allmers H, Schmengler J, Malte John S, et al. The disappearance of NRL-allergy in Germany and Europe. Presented at: Gloves Seminar; June 22–24, 2010; Spain and Italy. <http://www.mrepc.com/publications/seminar-papers.php>. Accessed May 30, 2011.
77. Allmers H, Schmengler J, Skudlik C. Primary prevention of natural rubber latex allergy in the German health care system through education and intervention. *J Allergy Clin Immunol* 2002; 110: 318–323.
78. Public Citizen: latex medical gloves a hazard. *DC Insider* April 26, 2011. <http://www.dcinsider.com/public-citizen-latex-medical-gloves-a-hazard>. Accessed May 30, 2011.
79. Switch! Change to powder-free, low-allergen latex gloves: experiences and recommendations from around the world. *Sempermed Informs* 2009; 7: 1–4.
80. Glove University. Donning powder and glove allergies. <http://www.gloveuniversity.com/allergies/powder.php>. Updated May 25, 2011. Accessed May 30, 2011.
81. US Food and Drug Administration. *Medical Glove Powder Report*. Silver Spring, MD: US Food and Drug Administration; September 2007. <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm113316.htm>. Updated June 18, 2009. Accessed May 30, 2011.
82. Jewell P. Powdered latex gloves: why their use is being phased out. University of Bath, Department of Biology and Biochemistry, July 2000. <http://www.bath.ac.uk/internal/bio-sci/bbsafe/latexgloves.htm>. Accessed May 30, 2011.

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