

Latex Allergy: Allergy Fact Sheet

By Dr. Kevin J. Kelly, MD, *Facts on Latex Allergy*

Allergy to Latex may be confusing and complex to diagnose and treat. There are three types of clinical reactions that occur to a finished natural rubber product.

1. **IgE mediated allergic reactions** (Type I) – This allergy may be life threatening and is the clinical problem that clinicians and patients are most concerned about preventing. This reaction is mediated by allergic antibody called IgE directed against retained proteins in latex products. This reaction is triggered by direct skin contact, mucosal surface contact or inhalation. Symptoms include hives, angioedema, rhinitis, conjunctivitis, asthma, or anaphylaxis with or without death.
2. **Cell mediated contact dermatitis** (Type IV) – This allergy is not life-threatening but is a major concern for clinicians and patients. This reaction is usually limited to the skin where contact occurs with rubber products. Multiple chemicals used in the manufacturing of latex products may be retained in the finished product. These chemicals include thiuram, carbamate, and mercaptobenzothiazole classes of compounds which are used to accelerate the cross-linking of isoprene in the manufacturing process. This contact dermatitis is a delayed type immune reaction mediated by T-cell lymphocytes that occurs with exposure to these chemicals and may take 24-48 hours to develop from the time of exposure to reaction. Symptoms of a rash with erythema, papules, vesiculation, and oozing are characteristic. Because the contact is usually repetitive, the rash may develop into a chronic problem and may even extend beyond the site of contact. It is important to note that this delayed-type contact allergy to chemicals may occur concurrently with IgE mediated allergic latex allergy.
3. **Irritant dermatitis** – Individuals who use rubber products frequently (e.g. health care workers who wear gloves) are subject to developing irritant dermatitis. This dermatitis is different from contact dermatitis. It is not mediated by an immune system sensitization and reaction. Rather, it is caused by frequent skin washing, sweating, and or irritation from powder lubricants from persistent irritant contact. This rash may be itchy but most commonly is dry, erythematous, and accompanied by skin cracking. There are rarely papules, vesiculation, or oozing of the skin. It never extends beyond the point of contact with the offending irritant.

Diagnosis: The diagnosis of latex allergy, contact dermatitis, and/or irritant dermatitis is made by a licensed independent medical provider who uses a medical history, physical exam and various laboratory and clinical tests. *Laboratory testing alone is insufficient to make a diagnosis.*

- Latex specific IgE antibody can be detected in a patient by skin testing or by blood tests. Latex skin testing reagents have not been cleared in the US Food and Drug Administration. Because skin testing has small but significant risk of adverse reactions in patients, careful consideration of the use of this technique for confirming a diagnosis of latex allergy is necessary when using uncharacterized skin test reagents.

IgE antibody can be detected by blood serum testing. The sensitivity of the FDA-cleared tests has been between 75-90%. The specificity of these serological



tests has ranged from 90-98% based on testing in subjects known to have latex allergy. When using this method to confirm a clinical diagnosis made by history and physical exam, the clinician must note that one of every four patients with latex allergic symptoms may have a false negative serology test. In contrast, when a history and physical exam are compatible with latex allergy and the serum test is also positive, then 95% of those subjects will have clinical symptoms with latex exposure. One of the major concerns about the serum assays is their ability to accurately detect latex allergic subjects as opposed to sensitized but asymptomatic individuals. The performance characteristics of the assays have been evaluated using subjects with known latex allergy. Assay performance may have more false positive tests if the population studied has a very low prevalence (such as 1%).

- Contact dermatitis is confirmed by the use of patch testing to the offending chemical.
- Irritant dermatitis is made by a medical history and physical examination alone.

Unexpected Clinical Manifestation of IgE mediated latex allergy: One of the unexpected manifestations of latex allergy has been the clinically evident allergic responses after ingestion or contact with select fruits and vegetables. It appears that as many as half of those individuals with primary latex allergy may develop clinical symptoms following ingestion of select foods (e.g., avocado, banana, kiwi). These reactions should not be surprising given the established laboratory cross-reactions seen between latex proteins and some food proteins. The converse appears to be true as well, in that those individuals with specific primary food allergies to certain fruits and vegetables may have allergic reactions to latex. This is estimated to occur in approximately 10% of food allergic individuals.

Treatment: Therapy for each of these conditions is individualized but essentially involves avoidance of the offending source that causes the reaction. In the case of IgE mediated allergy, personal contact with rubber products should be eliminated and a change of environment may be necessary if there is airborne exposure causing asthma. This is most prominent in settings that use cornstarch powdered latex gloves. Cornstarch powder serves as a carrier for allergenic proteins from latex. It may become airborne when the product is used. This may result in inhalation and subsequent allergic response in a sensitized patient. Thus, latex safety is complex. It is most important to note here that the latex products most likely to cause a reaction are those made by a dipping method (e.g. gloves, condoms, balloons) where the sulfur heat vulcanization process is relatively short and performed at a lower temperature. This allows the allergenic proteins to remain intact.

Latex Allergy: ANAPHYLAXIS Fact Sheet

By Dr. Kevin J. Kelly, MD, *Facts on Latex Allergy*

HOW TO RECOGNIZE ANAPHYLAXIS DUE TO NATURAL RUBBER LATEX:

- 1) Anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death.
- 2) Anaphylaxis to latex can occur in community settings (for example, after exposure to latex in balloons or other latex products) as well as in healthcare settings.
- 3) Anaphylaxis symptoms can occur within minutes after exposure to latex.
- 4) Anaphylaxis symptoms usually involve more than one body area at the same time. There may be only a few symptoms, or there may be many symptoms. Watch for:

Skin symptoms: itching, hives, redness, swelling

Mouth symptoms: itching, swelling of lips and/or tongue

Throat symptoms: itching, tightness/closure, hoarse voice, difficulty breathing

Lung symptoms: cough, wheeze, difficulty breathing

Gut symptoms: vomiting, diarrhea, cramps

Heart symptoms: weak pulse, dizziness, passing out

- 5) Anaphylaxis may occasionally have a second wave of symptoms (known as a biphasic response) requiring additional recognition and treatment.

HOW TO PREVENT ANAPHYLAXIS FROM NATURAL RUBBER LATEX:

- 1) Be able to identify the sources of natural rubber latex in the community such as balloons, sports equipment, or condoms.
- 2) Be able to identify the foods that cross-react with latex; for example, bananas, kiwi, avocado (see cross reactive food list in this document.)
- 3) Avoid exposure to natural rubber latex and the foods that cross-react with it except when an individual knows a specific food has been safe to eat.

HOW TO TREAT ANAPHYLAXIS FROM NATURAL RUBBER LATEX:

- 1) **Carry two epinephrine auto-injector devices with you at all times, and know how to use it. Inject epinephrine promptly in the middle, outer side of the thigh. Epinephrine is the life-saving drug in anaphylaxis.**
- 2) **Call for help promptly (911, EMS, rescue squad).**
- 3) Antihistamines such as Benadryl (diphenhydramine) and bronchodilators such as Ventolin (albuterol) should not be substituted for epinephrine in the treatment of anaphylaxis because they do not prevent or completely relieve anaphylaxis.
- 4) Have a personalized anaphylaxis emergency action plan (download from www.allergyasthmanetwork.org) and wear medical identification.

Latex Allergy: Asthma and Occupational Asthma Fact Sheet

By Michael Zacharisen, M.D., *Facts on Latex Allergy*

1 in 10 cases of asthma in adults is caused by or worsened by exposures at the workplace
Up to 18% of healthcare workers have natural rubber latex allergy
Women are more likely to be exposed to latex in their work than men.

Natural rubber latex products contain large rubber proteins from the rubber tree that can:

1. Stimulate the immune system to make allergic antibody (IgE) that can be measured in the blood.
2. Be carried on small particles and become airborne and inhaled into the lungs.

Sources of Airborne Latex: powdered, natural rubber latex (NRL) gloves, rubber balloons

At-risk jobs:

- Health care workers: physicians (especially surgeons), dentists, nurses, dental hygienists, dental and medical students and laboratory technicians.
- Professional cleaning and housekeeping staff
- Food handlers
- Hair dressers
- Workers making natural rubber latex products

Diagnosis: Establish the diagnosis of asthma AND latex allergy, then determine whether asthma is triggered by latex.

- Asthma symptoms (cough, wheeze, chest tightness, shortness of breath)
- Location: initially symptoms occur at the workplace and improve away from work, on weekends, and while on vacation; however, over time, symptoms can become persistent
- Examination by a physician skilled in the evaluation of asthma and occupational diseases
- Chest x-ray: helps eliminate the possibility of other lung problems, but frequently is normal
- Spirometry: simple breathing test that can establish air flow obstruction. Repeat spirometry test after inhaling albuterol can determine if lung function improves.
- Methacholine challenge: a breathing test to help confirm asthma when spirometry is normal.
- Peak flow: very simple handheld device to check peak expiratory flow rate before, during, and after work to determine if lung function decreases at work and improves away from work.
- Latex allergy: obtain blood test for latex specific IgE to confirm latex allergy. Elevated levels of IgE to certain latex proteins (recombinant Hev b 5 combined with recombinant Hev b 6.01 or 6.02) are highly predictive of latex-induced asthma.

Treatment:

- Identification of latex allergy and asthma in the early stages in an effort to reduce latex exposures as well as prevent and treat symptoms is the key to improved long-term outcomes.
- Avoid and/or reduce airborne latex: substitute powdered latex gloves with low protein powder-free gloves or latex-free gloves
- Avoid rubber balloons and processes where latex products are produced
- Once a person is allergic to latex, other irritants like smoke and fumes can aggravate asthma
- Using face masks can reduce latex exposure, but does not completely prevent latex asthma
- Treat asthma with usual asthma medications
- Desensitization protocols for latex allergy are currently experimental. Latex immunotherapy injections were associated with an unacceptable high risk of side effects. Sublingual immunotherapy (drops under the tongue) have shown promise in small clinical trials with less side effects, but lack of a current latex extract is delaying implementation.

Latex Allergy:

Latex Allergy Information Fact Sheet

By Dr. Kevin J. Kelly, MD, *Facts on Latex Allergy*

- Natural Rubber Latex is a milky liquid produced by lactiferous plants or trees.
- There are >2000 lactiferous plants in the world.
- The major source for NRL is from the Hevea Brasiliensis tree and is used to make numerous commercial and medical products.
- NRL contains a highly cross-linked polymer with a structure of cis 1,4 polyisoprene.
- Manufacturers utilize heat vulcanization with sulfur to cross-link the polyisoprene.
- The vulcanization may be performed at a lower temperature and shorter duration by using accelerators in products made by a dipping method (e.g. medical gloves) while high temperature and prolonged duration is used for other types of rubber (e.g. car tires).
- This unique structure creates a strong, elastic barrier that tends to be virtually impermeable to water and that returns to its original shape after multiple stress forces are applied.
- The polyisoprene is immunologically inert and is not known to cause allergic reactions.
- Approximately 2% of the weight of NRL is from proteins that are produced in the lactifer plant.
- 13 of these proteins have been well characterized and known to result in IgE mediated allergic reactions.
- Most of these allergic reactions have been reported to occur from finished rubber products that are made by a dipping method with formulated natural rubber latex.
- Approximately 12% of the NRL harvested is used to make products by this dipping method.
- Manufactured latex products may contain additive chemicals that either accelerate the cross-linking or are anti-oxidants used in the process. Many of these chemicals have a propensity to cause delayed hypersensitivity reactions manifested as contact dermatitis.
- Thiurams, carbamates, and mercaptobenzothiazole chemicals are the most common rubber additive chemicals to cause contact dermatitis.
- Allergic contact dermatitis is clinical diagnoses made by a licensed independent health care provider that utilizes a medical history, physical exam, and possibly patch skin testing to the offending agent.
- Some individuals who develop IgE mediated latex allergy also have preceding or concurrent contact dermatitis.
- Many workers (possibly 30%) who use latex gloves and other gloves may get irritant dermatitis on their hands from numerous causes (e.g. sweating, powder, frequent hand washing).

- This dermatitis may precede or be concurrent with the development of IgE mediated latex allergy.
- A diagnosis of irritant dermatitis is a clinical diagnosis made by a licensed independent health care provider that utilizes a medical history and physical exam.
- IgE mediated latex allergy to NRL may cause hives, angioedema, rhinitis, conjunctivitis, asthma, and anaphylaxis with or without death.
- The allergenic proteins in latex may be carried on cornstarch powders that are used as a lubricant on some gloves resulting in respiratory exposure to patients and workers.
- Patients with spina bifida, cloacal anomalies, multiple surgeries, diabetes on insulin injections, and atopic subjects appear to be at a higher risk of developing latex allergy.
- Individuals in occupations where latex gloves are worn may develop symptoms of IgE mediated latex allergy more frequently when compared to other occupations where latex is not used.
- The definitive cause of the latex allergy epidemic in spina bifida and health care workers in the 1990's is not clear. Prevalence studies and avoidance strategies suggest that allergen content of latex gloves as well as inhaled latex allergen on powder from latex gloves may have contributed strongly to symptoms.
- Blood donor studies suggest that up to 8.2% of the general population may have detectable IgE antibody directed against latex allergen. This does not mean that 8% of the population has latex allergy. Two large cohorts of subjects skin tested to latex in Europe have shown the prevalence of positive skin test to be approximately 1%.
- Approximately 50% of latex allergic subjects show laboratory or clinical symptoms of allergy (cross-reactivity) to one or more fruit.
- Bananas, avocados, kiwi, and stone fruits appear to elicit the most clinical cross reactivity.
- Approximately 10% of fruit allergic individuals may have cross-reactivity to NRL
- A skin testing reagent of natural rubber latex has not been cleared by FDA in the US. It should be noted that a well characterized skin test reagent has not resulted in severe untoward reactions. However, the use of non standardized latex reagents has occasionally resulted in severe allergic reactions in those subjects tested.
- Serologic testing for the presence of anti-latex IgE antibody has a sensitivity of 75-90% depending on the type of assay and substrate antigen.
- The specificity of the serologic assays for the presence of anti-latex IgE antibody has a specificity of 90-98% depending on the type of assay and substrate antigen.
- Serologic assays may result in false negative responses in 10-25% of subjects tested.
- Serologic assays may result in false positive responses in a significant proportion of subjects tested depending on the prevalence of the disease.
- The diagnosis of latex allergy is a clinical diagnosis made by a licensed independent health care provider that utilizes a medical history, physical exam, and possibly skin testing or serologic testing.

Latex Cross-reactive foods

Fact sheet update

By Tom Grier, *Facts on Latex Allergy*

Allergic reactions to products containing natural rubber latex often result from exposure of sensitized individuals to one or more proteins that occur naturally in raw latex preparations. At least 14 distinct proteins have been identified and associated with latex sensitivities in health care workers, spina bifida patients, and symptomatic children or adults within the general population, with most allergic patients reacting to multiple latex proteins that vary somewhat between these groups.

The biological functions or enzymatic activities associated with most latex allergens have been determined. Several of these proteins are active enzymes involved in defending the latex plant from microbial attacks, particularly colonization and growth of numerous fungi. In general, proteins that serve similar functions in different plants (whether genetically related or not) usually contain highly conserved sequences and structures, so it is not surprising to find plant defense or pathogenesis-related proteins with activities comparable to those found in latex in a variety of plants that include many common foods.

These relationships are relevant to latex allergy because a number of these common plant defense proteins are potent allergens. The tendency of latex-sensitive individuals to express allergic reactions after ingestion of certain foods has been recognized for many years, and subsequent clinical and laboratory studies have confirmed both the sources of the offending allergens and their relevance to the allergic condition. Our immune systems recognize particular antigen structures as foreign without regard to the origin of these molecules. Close structural similarities between any two allergens from divergent sources can produce similar allergic reactions in sensitive patients, and is termed cross-reactivity or cross-sensitization. Ingestion of some foods produce allergic symptoms in patients sensitive to latex inhalation or contact due to the presence of these common or cross-reactive protein allergens.

This association between latex sensitivity and food allergy is often referred to as the latex-fruit syndrome, although many vegetable foods have also been identified as possessing clinical and/or immunologic cross-reactivities with latex proteins. The foods shown below have been linked allergenically to latex in published reports and are grouped based on high, moderate or low/undetermined degrees of association to latex or prevalence of allergic reactions. It is likely that other foods not yet identified also possess some allergenic similarities to latex.

High (4) Avocado, Banana, Chestnut, Kiwi

Moderate (7) Apple, Carrot, Celery, Melons, Papaya, Potato, Tomato

Low/undetermined (40) Apricot, Buckwheat, Cassava/Manioc, Castor bean, Cherry, Chick pea, Citrus fruits, Coconut, Cucumber, Dill, Eggplant/Aubergine, Fig, Goji berry/Wolfberry, Grape, Hazelnut, Indian jujube, Jackfruit, Lychee, Mango, Nectarine, Oregano, Passion fruit, Peach, Peanut, Pear, Peppers (Cayenne, Sweet/bell), Persimmon, Pineapple, Pumpkin, Rye, Sage, Strawberry, Shellfish, Soybean, Sunflower seed, Tobacco, Turnip, Walnut, Wheat, Zucchini

It is important to note that some of the foods on listed above may not produce clinically important reactions in latex-sensitive individuals, for numerous reasons. However, recognition of the foods that are known to share some major or minor allergens with latex can help patients and their families minimize exposures to possible sources of provocative allergens and understand the risks associated with inclusion of these foods in their diets.

