REVIEW

Latex Allergy: Position Paper

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Abstract

Correct management of latex allergy is essential to ensure adequate care of patients who are allergic to latex, which is ubiquitous in the health care setting. In this Position Paper, the Latex Committee of the Spanish Society of Allergology and Clinical Immunology provides guidelines for the management of latex allergy.

Key words: Latex allergy. Guidelines.

Resumen

El correcto manejo de la alergia al látex es fundamental para garantizar la buena atención de este colectivo de pacientes, dada la ubicuidad de este alergeno en el medio sanitario. El comité de alergia a látex de la SEAIC con este documento de posición pretende resumir de forma clara las directrices a tener en cuenta en esta patología.

Palabras clave: Alergia a látex. Recomendaciones.

Introduction

Natural rubber is obtained from the *Hevea brasiliensis* tree. It takes the form of a milky aqueous suspension and is extracted by making cuts in the tree bark. Stabilizers and preservatives are then added to prevent it from coagulating [1,2,3].

Rubber products are obtained using 2 different processes: latex concentration and production of natural dry rubber. After harvesting, the latex is centrifuged to obtain 60% dry rubber. Vulcanization accelerators, antioxidants, and other substances are then added, depending on the final characteristics to be obtained [4]. This latex is used to manufacture the objects most frequently associated with allergic reactions such as gloves, condoms, balloons, and catheters [5,6]. In the case of natural dry rubber, the latex is coagulated by reducing its pH with formic acid and acetic acid to produce rubber in the form of sheets or bales, which then undergo 3 phases: malaxation (with additives), moulding, and vulcanization (a type of polymerization which creates a hard, crystalline structure). In this type of processing, the protein content is lower, and vulcanization denaturalizes the proteins that remain. [2]. This type of latex is used to manufacture health care products such as stoppers for tubes, pistons, masks, and cannulas [5,6].

History of Latex Allergy

Type IV hypersensitivity to latex additives is well documented and does not differ from other types of contact dermatitis [7]. The first cases of latex allergy through type I hypersensitivity were described in 1927 in Germany [8] and then in 1979 [9]. In Spain, the first case was published in 1986 [10]. In the 1980s, the number of cases reported increased considerably, mainly as a result of the confluence of 3 factors [5,6,11]:

– Widespread use of latex gloves
– Simplification of the manufacturing process
– Substitution of talcum powder with starch to prevent the formation of granulomas. (Starch is an extremely efficient vehicle for the diffusion of allergens).

Latex allergy has become a major health problem. The alarming increase in latex-induced anaphylactic reactions during operations or radiological procedures prompted the United States Food and Drug Administration to publish a series of recommendations on the issue in 1990 [12]. In addition, the protein content in gloves was lowered to reduce allergenicity [13]. These measures, together with the prevention strategies implemented in countries such as Germany [14,15], partly halted the epidemic. However, in developing countries, the incidence of cases is increasing as latex products are more widely used [5].

Latex Allergens

Fourteen allergens have been identified (www.allergen.org). Given its plant origins, latex has panallergens and constitutive allergens. In addition, allergens are generated during the manufacturing process (vulcanization). The different allergens sensitize patients in several risk groups through various routes of exposure. Clinical pictures vary, although there is frequently some degree of overlap [16-19].

The allergens characterized to date are as follows:

- Hev b 1, or latex elongation factor [18], is a 14-kDa protein involved in the synthesis of polyisoprene. It is a major allergen in patients with spina bifida (54%-100%) and a secondary allergen in health care workers. As it is not soluble in water, its availability by inhalation is low.
- Hev b 2 is a secondary 34-kDa allergen belonging to the plant defense proteins group. Depending on the geographical region, 5% to 15% of allergic patients are sensitized. No differences in sensitization have been recorded between patients undergoing multiple operations and health care workers [20].
- Hev b 3 belongs to the rubber particles group and has a molecular weight of 24-27 kDa. It shares its biological function with Hev b 1 and, like Hev b 1, it is insoluble and the major allergen in patients with spina bifida (77%-100%) [21,22]. These allergens cross-react.
- Hev b 4 is a protein with a microhelix of 50-57 kDa. Its clinical relevance is as yet undetermined, although it sensitizes 39% of health care workers [23].
- Hev b 5 is an acid 16-kDa structural protein whose biological function is unknown. It is the main allergen in different risk groups and is recognized by 92% of health care workers and 56% of patients with spina bifida [24]. For reasons that remain unclear, its prevalence varies from region to region. Hev b 5 presents multiple isoforms and exists in very small amounts in non–amino acid extracts such as those used in diagnosis. Its addition to ImmunoCAP (Phadia) increased the sensitivity of the technique [25]. Hev b 5 shows homology with the kiwi acid protein [26].
- Hev b 6, or prohevein (hevein precursor, Hev b 6.01) is a 20-kDa allergen that belongs to the class I chitinases. It has a defensive function, as it degrades chitin, a component in the cell walls of fungi and the exoskeleton of insects. Processing leads to 2 allergenic fragments, the N-terminal or hevein (Hev b 6.02) and the C-terminal (Hev b 6.03), which act independently. Hevein is the more important of the two and is a major allergen whose prevalence is greater in health care professionals than in patients with spina bifida [19]. Its sequence shows >50% identity with chitinases from fruits such as banana, avocado, and chestnut, thus giving rise to the latex-fruit syndrome, which is included in cross-reactivity syndromes [27].
- Hev b 7 is a 43-kDa protein that is more than 50% homologous with patanin, a storage protein in *Solanaceae*, thus explaining the cross-reactivity with these plants. Hev b 7 is recognized by 23% to 45% of patients [19,23] and is therefore a relevant—but not major—allergen.
- Hev b 8 is latex profilin. This secondary 14-kDa allergen belongs to the profilins, a group of panallergens that are widespread in plants and that could be responsible for cross-reactivity with exotic fruits such as kiwi and avocado. Although its role as a sensitizing airborne allergen has been questioned in health care workers, it should be taken into account for the correct interpretation of specific immunoglobulin (Ig) E to latex in pollen-sensitive patients. Cross-reactivity may exist between Hev b 8 and pollen profilins; therefore, specific antibodies against latex may have no clinical relevance [28].
- Hev b 9 is a 52-kDa enolase that cross-reacts in vitro with enolase from fungi of the genera *Cladosporium* and *Alternaria*. Its clinical importance is debatable [29].
- Hev b 10 is a secondary 26-kDa allergen with a superoxide-dismutase function and homology with enzymes of the same function in *Aspergillus*. It seems to have no clinical relevance [30].
- Hev b 11 is a secondary 30-kDa allergen belonging to the class I chitinase group [27]. Cross-reactivity with hevein (Hev b 6.02) is low, and its involvement in cross-reactivity with fruits is unknown.
- Hev b 12 is a secondary 43-kDa lipid transfer protein and Mediterranean plant panallergen that is included in the defense proteins group. No conclusive data exist regarding its possible cross-reactivity with foods [31].
- Hev b 13 is a 42-46–kDa secondary allergen, although its prevalence has been reported to be 18%-27% [17]. It mainly affects health care workers and, as such, is a relevant allergen.
- Hev b 14, also known as hevamine, is a 30-kDa allergen belonging to the chitinase group. Its clinical relevance remains to be determined [32], although it has been identified as a major allergen in the Taiwanese population [33].

The main characteristics of the allergens in terms of clinical relevance are summarized in Table 1.

The commercially available ImmunoCAP test can be used to determine specific IgE against the recombinant antigens Hev b 1, 3, 5, 6.01, 6.02, 8, 9, and 11. Specific IgE to rHev b 1,

Table 1. Clinical Relevance of Latex Allergens

Allergen	Property
Hev b 1 and 3	Main allergen in spina bifida
Hev b 5 and 6	Main allergen in health care workers
Hev b 2, 4, 7, and 13	Secondary but relevant allergen in health care workers
Hev b 6.02 and 7	Verified cross-reactivity with fruits
Hev b 8, 11, and 12	Panallergens with unknown cross-reactivity with fruits

rHev b 3, rHev b 5, rHev b 6.01, and rHev b 8 is determined using the The hypersensitivity profile of each patient also has therapeutic implications, as the only commercially available vaccine against latex contains the allergens Hev b 5 and 6.

Measurement of Environmental Exposure

Studies quantifying environmental concentrations of airborne latex allergens have been carried out in different health care and hospital environments, ambulances, dental clinics, industrial latex processing plants, as well as on objects used in health care and daily life and in samples of air from urban areas [34,35-50]. The environmental concentrations of the airborne allergens of latex capable of sensitizing and producing symptoms are not well defined, given the complex mixture of potent allergens with differing stability and bioavailability that make up latex, their widespread presence [34], and the lack of sufficiently solid studies [35,51-53]. Increased frequency of sensitization has been associated with concentrations greater than 0.6 ng/m^3 in the air of hospital rooms [47]. A concentration of 10 ng/m^3 has been proposed as the threshold level for health care environments [37].

Latex allergens are proteins that adsorb to the dust particles present on latex objects. They are aerosolized and behave as airborne allergens of different particle sizes, although most (80%) have a mean diameter >7 μm and a high molecular mass. As the 2 main routes of exposure to latex are the respiratory mucosa and the skin, both environmental air and surfaces should be monitored [53]. Latex allergens may be present as individual particles or may adhere to the surface of other particles [54-63].

Measurement of the Amount of Protein in Latex Objects

Samples from surfaces may be collected using 3 techniques:

1. By simply collecting the sample with tweezers and storing it in a sterile container or bag
2. By passing a polytetrafluoroethylene (PTFE) filter over the surface in question in order to trap the allergens
3. By aspirating the surface

No suitable method exists for measuring latex allergens in manufactured products; therefore, the amount of latex protein that can be extracted should be determined.

None of the methods available provides data on the allergenicity of the proteins detected. The modified Lowry method has become the standard, and the analysis of amino acids is also used for some products. Both approaches are used to compare brands. In addition, both methods are used to detect the total amount of proteins present, but do not rule out the presence of residual latex allergens and do not distinguish other proteins that may have been added to the product [57]. Both have been standardized according to European norm UNE-EN-455-3 [58].

The Lowry method is relatively inexpensive and simple. The limit for detecting and extracting total protein from latex gloves has been established at 10 mg per glove, the equivalent of 2 mg/mL of extract, depending on the weight of the glove (European Committee for Standardization) [58].

Amino acid analysis can be used in latex products other than gloves. As it is more sensitive, it can be used to approximate threshold exposure levels.

Methods of measuring specific allergens have not been validated and are not readily available. It is difficult to adapt them for use in industrial plants producing latex or those manufacturing finished products. The protein content of gloves is very variable and ranges from 0 to >1000 mg/g of glove [59]. Results obtained by measuring the total amount of latex protein with the Lowry method have been found to correlate with the biological activity of the latex extracts from gloves [60-63]. Thus, using this method, allergenicity has been associated with low, moderate, and high protein content values [64]. These criteria may be important in the prevention of sensitization to latex.

Measurement of the Amount of Protein in the Air

The environmental concentration of airborne latex allergens is measured by taking samples of environmental air using air samplers in which the latex allergens can be extracted from the filters [34,36-38,41,46]. The samples obtained can be analyzed quantitatively and qualitatively using immunochemical methods [65-67]

An appropriate filter must be used to obtain the desired results. The most suitable filters are those composed of PTFE (Quan-Tec-Air).

Clinical Syndromes

Clinical manifestations induced by type I hypersensitivity reactions to latex proteins vary greatly [68-70] and depend on the route of exposure, the amount of allergen, and individual factors.

Contact Urticaria

Contact urticaria is the most frequent manifestation and may be the only manifestation or that preceding systemic manifestations.

Eczema and xeroderma following glove use are nonspecific symptoms [70]. Urticaria is more highly correlated with sensitization to latex than isolated pruritus [71-73].

Contact with the mucosa induces angioedema.

Latex is the most common cause of occupational contact urticaria [74]. Dermatitis of the hands caused by irritants may foster sensitization to latex. Urticarial lesions that are mediated by type I hypersensitivity to latex proteins and become chronic could result in protein contact dermatitis [74]. Clinically, protein contact dermatitis manifests as chronic eczema with episodes of recurrent acute attacks. It represents a combination of immediate-type hypersensitivity (type I) and delayed-type hypersensitivity (type IV).

Allergic Rhinitis and Asthma

Allergic rhinitis and asthma mainly affect individuals exposed via inhalation, such as health care professionals and workers who use protective gloves or who are exposed to latex in their work environment [40,70,75-84]. Powdered gloves are the main source of reactions to environmental latex [10,69,75,69,85-88].

Latex is considered to be an occupational allergen [34,88-94] and is the cause of occupational asthma in the professions affected, with a prevalence of between 2.5% and 10% [94-98].

Eosinophilic bronchitis due to latex is an infrequent occupational respiratory manifestation [99].

Systemic Reactions

Latex is the second cause of intraoperative anaphylaxis after muscle relaxants [100,101]. The frequency of perioperative anaphylaxis attributed to latex has remained relatively stable in recent years, with a slight increase according to recent data: a minimum of 12.1% was reached in 1997-1998 and a maximum of 22.3% in 2001-2002 [102].

Cardiovascular collapse is the most common form of presentation in anesthetized patients, although skin rash and bronchospasm are also frequent [100-103].

Reactions to latex normally occur during the maintenance phase of anesthesia, unlike anaphylaxis due to muscle relaxants and opiates, which is more frequent in the induction phase. Abdominal, gynecological, and orthopedic operations present the greatest risk [104-108], although barium contrast enema and anorectal manometry should also be borne in mind [109-111].

In children, latex is involved in 27% of anaphylactic reactions following anesthesia, with higher figures in those aged under 5 years [105]. The population at risk of suffering an anaphylactic reaction to latex after an operation or medical examination can be divided into individuals with a genetic predisposition (atopic) or individuals with higher levels of exposure (health care workers and patients undergoing multiple operations or tests) [106].

Latex proteins from gloves can be transferred to food handled using gloves. These proteins can cause anaphylactic reactions in sensitized individuals who subsequently consume the food [111-113]. To avoid latex acting as a hidden allergen in such cases, the Spanish Agency of Food Safety and Nutrition (Agencia Española de Seguridad Alimentaria y Nutrición) has issued a recommendation to avoid the use of latex gloves in food companies [114].

Latex-Fruit Syndrome

Latex-fruit syndrome involves cross-reactivity between inhaled and food allergens [115-121]. Anaphylaxis to both latex and foods is common [115,122-125] and may be the initial manifestation.

The clinical features of latex-fruit syndrome have been described by different authors in different countries [126-131] and can be summarized as follows:

(a) The association between latex allergy and fruit allergy ranges between 21% [120-130] and 58% [116,126]. This variability can be explained by the differences in diagnostic criteria and eating habits [118,126]. The frequency of sensitization to foods without symptoms is very high [128].

(b) The foods most frequently involved are chestnut, avocado, banana, and kiwi, although many others are involved [118,119,127,128].

(c) The spectrum of clinical reactions to foods is very wide. The proportion of anaphylactic reactions caused by foods ranges from 50% [115] to less than 5% [119]. Banana, avocado, chestnut, and kiwi are associated with anaphylaxis [115,118]. Other foods (eg, fig, papaya, and tomato) are more infrequently associated with latex allergy, although they can also cause anaphylactic reactions. In contrast, foods such as potatoes can occasionally cause mild local reactions [118].

Although latex allergy precedes hypersensitivity to foods in most patients, the reverse may also occur. Several studies have shown that, in many cases, the spectrum of food allergies may increase over time [115,120].

Among the main latex allergens, class I chitinases, which have a hevein N-terminal domain, have been considered responsible for latex-fruit allergy syndrome [42], although other plant panallergens that are present in latex, such as glucanase (Hev b 2), profilin (Hev b 8), LTP (Hev b 12), or even isolated hevein domains, may play an important role [129,130].

Clinical Manifestations in Spina Bifida

The prevalence of latex allergy is greater in children with spina bifida than in the general population [131,132]. The fundamental risk factor is the number of operations [133-135]. Other factors, such as elevated IgE titers, presence of a ventriculoperitoneal shunt during the first days of life, and atopy also increase the risk [136-139].

Exposure to latex in these children is via several routes (mucosa, blood vessels, and inhalation).

The most frequent manifestation is urticaria-angioedema, in contrast with health care workers, who exhibit respiratory symptoms. The most relevant allergen appears to be Hev b 1 [140].

Diagnosis of Latex Allergy (Figure 1)

Diagnosis of latex allergy is based on clinical suspicion, although this is not always easy to establish [7,141,142]. The sensitivity and specificity of a good clinical history taken by an experienced allergologist are very high [143]. The history should record the presence or absence of other allergies, atopy,

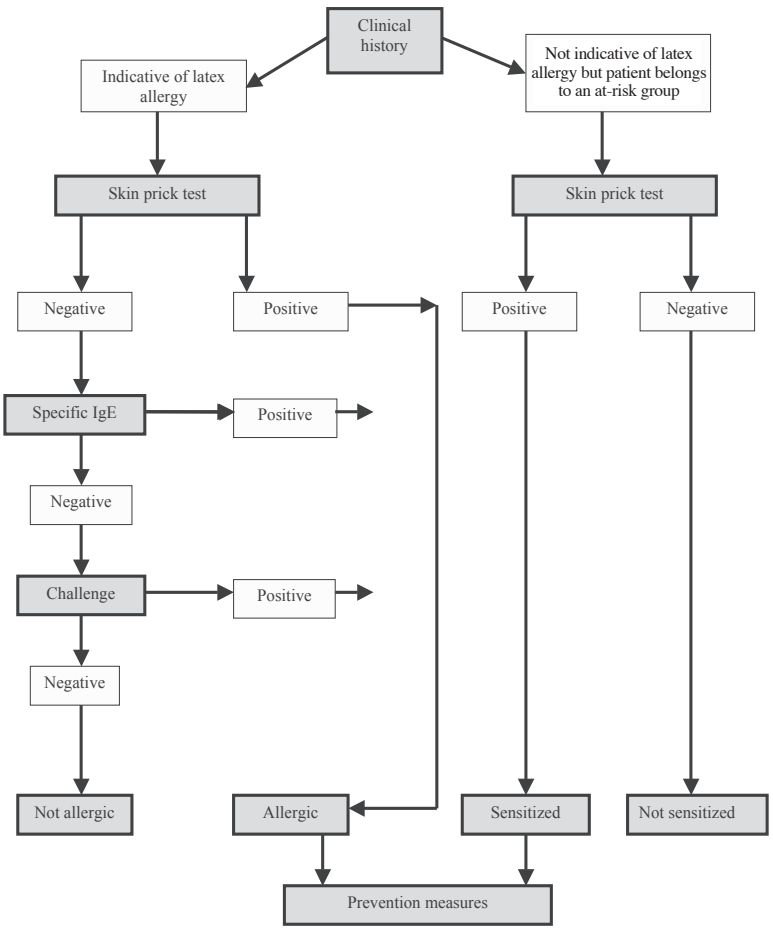

Figure 1. Diagnostic algorithm for latex allergy. Ig indicates immunoglobulin.

previous operations or medical procedures involving latex products, and whether the patient belongs to an identified risk group [144,145]. Exhaustive questions should be asked regarding the possible source of exposure [146], and note should be taken of the existence of any acute episodes of anaphylaxis or urticaria with no known cause. Finally, patients should be questioned about reactions induced by contact with or ingestion of fruit, particularly kiwi, chestnut, avocado, and banana [115].

Specific questionnaires may be useful, thanks to their high sensitivity, although they lack specificity. They are especially useful in the identification of sensitized and asymptomatic patients belonging to high-risk groups [144] and in studies of prevalence [147].

The complementary diagnosis is based on skin tests and the determination of specific IgE using the different methods available. A positive result in any of these may be considered indicative of sensitization to latex [148], that is, the presence of specific IgE antibodies, although, as these can be detected in asymptomatic individuals, the results should not be analyzed without the clinical history.

Skin Tests

Prick tests

Prick tests are considered the method of choice to confirm or rule out latex allergy [150]. Standardized extracts can provide a sensitivity of 93% with a specificity of 100% [151-153] and are considered safe, although isolated cases of anaphylaxis have been reported [154]. Intradermal tests are not recommended.

Patch tests

Patch tests are used in suspected delayed-type hypersensitivity reactions, most of which are not attributable to latex but to additives. With the exception of mercaptobenzothiazole and N-I-para-phenylenediamine, it is advisable to test mixtures of substances (carba mix, paraphenylenediamine mix, and thiuram mix) instead of each additive separately [154-158]. Latex patches without additives are not recommended [156], although exceptional cases of contact dermatitis due to latex itself have been reported in negative prick tests [154,157-160].

Laboratory Tests

Determination of specific IgE against latex

Sensitivity using CAP (Phadia) or AlaSTAT (Diagnostics Products Corporation) is high [161-163]; however, it may vary widely between the different methods available, especially when high-risk populations such as health care workers are analyzed and the clinical history is not taken into account [141,164]. When the clinical history is taken into account and a positive cutoff point is established at >0.35 kU_A/L, both techniques show similar sensitivity (97% and 100%, respectively) with specificities of 83% for CAP and 33% for AlaSTAT [165,166].

Determination of recombinant allergens using CAP may confirm the diagnosis in cases where sensitization has not been proven by other techniques and is useful for establishing profiles of sensitization to different allergens in different groups of patients [167]. Another means of detecting specific IgE is by ImmunoCAP ISAC (CRD 112) (Phadia), in which the components of purified allergens are fixed on a biochip. In a 2-phase assay, the antibodies from the patient's serum bind to the components of the fixed allergens. After a brief washing phase, the antibodies bound to the allergens are detected using a fluorescent antibody. The results of this semiquantitative test are expressed in ISAC standardized units. The latex allergens available are rHev b 1, rHev b 3, rHev b 5, rHev b 6.01, and rHev b 8. Immunoblotting can also be used to detect specific IgE, but always as a complement to another diagnostic technique [168].

Flow cytometry

Flow cytometry has proven efficient in the diagnosis of latex allergy [169-172], even in children and using recombinant allergens [171], with a sensitivity greater than 93% and a

specificity of 91.7% [172,173]. The technique is not widely used, given its high cost.

Challenge Tests

Challenge tests are indicated when the clinical history is suggestive and complementary diagnostic tests (skin or laboratory tests) are negative or contradictory [6]. They may also be used to rule out latex allergy in asymptomatic sensitized patients.

Rubbing test

The rubbing test gives false positives and is not standardized. Thus, its diagnostic yield is very low and it is not used [174].

Glove use test

Considerable disparity exists between glove use protocols, with exposure times ranging from 15 minutes to 2 hours. In general, the first step involves placing a fingertip of the glove on a dampened finger; if the result is negative, the complete powdered glove is put on. A vinyl or nitrile glove is used on the other hand as a negative control. The result is considered positive if contact causes erythema, pruritus, blisters, or respiratory symptoms.

The main limitations of the glove use test are the difficulty in blinding, thus favoring false positives, and the existence of false negatives, especially in patients who have avoided latex for a long time. The test has been used in different groups of patients, including children with spina bifida [175,176].

Specific bronchial challenge test

Bronchial challenge tests have been performed using different methods and are classified into those that use an aqueous latex extract (with a nebulizer or in a chamber with aerosolized glove extract) and those consisting of handling or shaking gloves to generate a dust aerosol [177-183].

Conjunctival challenge [184] and nasal challenge [185] have also been used, although they are generally of little value.

Diagnosis of Food Allergies Associated With Latex Allergy (Figure 2)

Skin prick test with the fresh fruit involved in the latex-fruit syndrome shows 80% agreement with the clinical diagnosis and is a simple, inexpensive, and reproducible way to confirm clinical suspicion. If the different fruits are analyzed separately, agreement is lower with papaya and kiwi (around 60%) than with banana, avocado, and chestnut (close to 90%). The commercially available extracts with the fruits involved in the syndrome have a diagnostic sensitivity lower than that of the prick test, probably due to a lack of standardization [128].

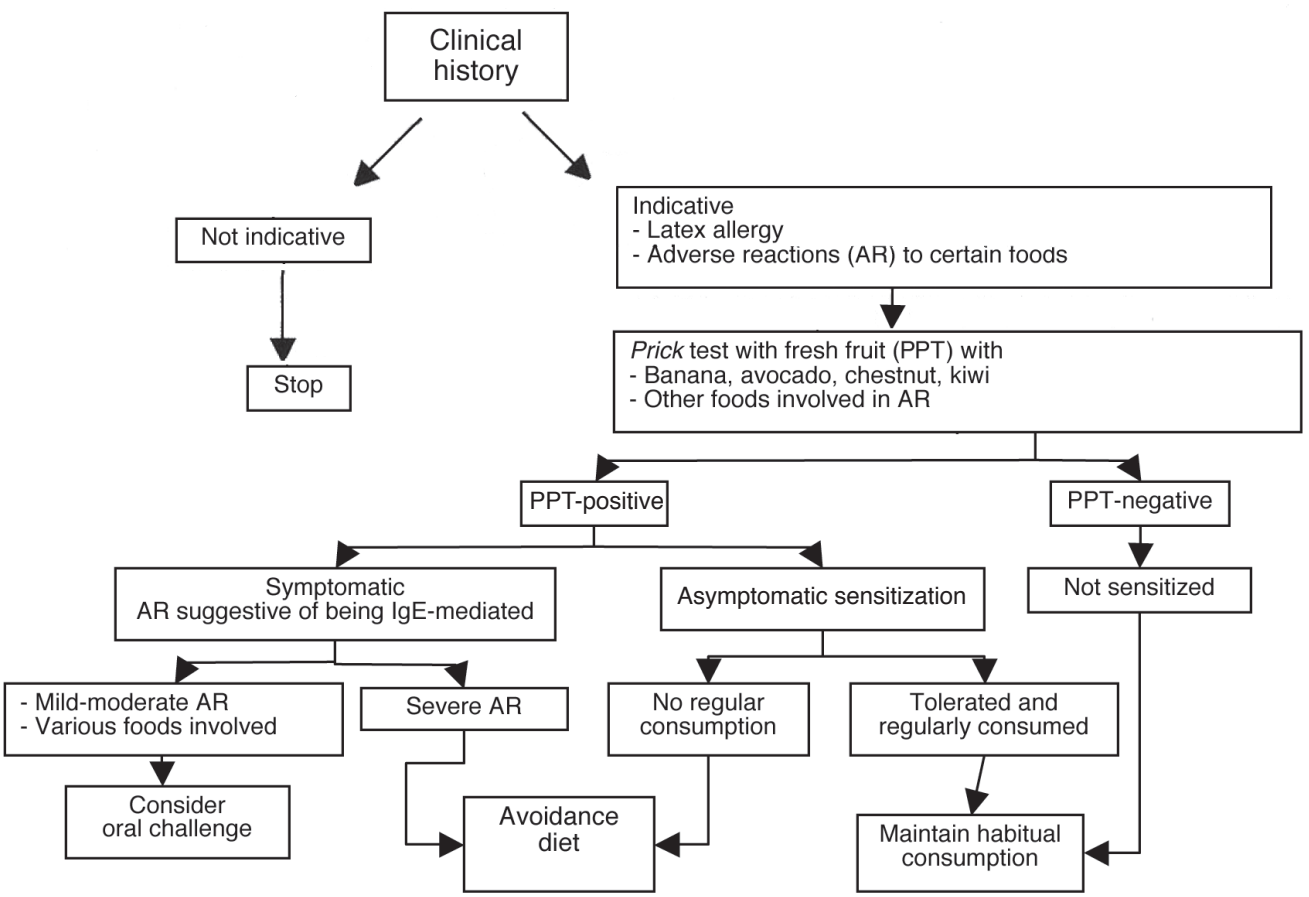

Figure 2. Example algorithm for the diagnosis and treatment of latex-fruit allergy syndrome. PPT indicates prick-prick test; AR, allergic rhinitis.

Similarly, the diagnostic sensitivity of specific IgE against fruits using the CAP method is substantially lower than that of the clinical history and the skin prick test with fruit. Determination of specific IgE against avocado (near 80%) is better than against the other fruits involved [119,128].

Treatment

The mainstays of management of latex allergy are treatment of the present reaction and prevention of future reactions.

Patients with allergic reactions to latex should receive standard treatment (depending on severity) using latex-free material in a latex-free environment. Patients must be reminded of the importance of carrying an epinephrine self-injector. Neither of the 2 self-injectors commercially available in Spain—Altellus and Jext—contains latex.

However, it is also important to implement adequate measures to avoid future reactions, namely, patient education, avoidance of contact with latex objects, and treatment with specific immunotherapy.

Patient Education

Patients must understand the importance of identifying themselves as allergic to latex and knowing where latex may be present and how to avoid it (see *7.2. Avoidance of Latex Objects*). This precaution is particularly important in the health care setting. If a patient is admitted to hospital, latex allergy should be stated clearly and unequivocally in the clinical history, the nursing notes, the surgical report (where applicable), and at the head of the patient's bed. Furthermore, patients should wear a medical bracelet warning of the danger.

Avoidance of Latex Objects

Full avoidance of latex is considered impossible, given its widespread use [186,187], although it is frequently not necessary in most allergic patients, who tolerate exposure to everyday rubber objects [62,188].

Table 2. Objects Used in Health Care Settings That May Contain Latex[a]

Catheters
Syringes
Stoppers
Elastic bandages
Drains
Respirator tubes
Tourniquets
Nasogastric tubes and catheters
Compression stockings
Masks
Balloons
Handles
Footwear
Ventriculoperitoneal shunt
Stethoscope tubes

[a]The list is not exhaustive.

Table 3. Commonly Used Objects Containing Latex[a]

Adhesives
Balloons
Nonslip mats
Condoms
Contraceptive diaphragms
Baby bottle nipples
Pacifiers
Shoes
Gloves
Diapers
Elastic tissues
Elastic bands

[a]The list is not exhaustive.

Avoidance measures are also implemented in patients with suspected latex allergy pending confirmation [189]. The written information given to latex-allergic patients about their illness must include a list of objects that could contain latex (Tables 2 and 3) and details of suitable alternatives, including latex-free gloves and condoms.

For further details, see *8.3 Secondary Prevention*.

Alternatives to latex for the manufacture of gloves and other medical products

Alternatives to latex exist for most rubber objects and include neoprene, polyvinyl chloride, silicone, polyurethane, and vinyl. In the case of medical devices, alternatives can be found in different publications and on the Internet (www.latexallergylinks.tripod.com, www.latexallergy.ndo.co.uk, www.latexallergyresources.org).

Most important is the substitution of latex gloves, the main source of latex allergens in the health care setting. Not all the alternatives are suitable for all the procedures carried out in hospitals.

Polyvinyl chloride (or simply vinyl) gloves do not have the same barrier effect as latex gloves [190-193] and, as such, are not a valid alternative as protection against infection. Nitrile

Table 4. Characteristics of Gloves for Health Care Use[a]

	Latex	Nitryl	Neoprene	Vinyl
Resistance	5	5	5	1
Biological protection	5	5	5	2
Chemical protection	4	5	5	1
Elasticity	5	3	4	1
Comfort	5	2	4	3
Sensitivity	5	2	4	3
Price	3	2	1	5

[a]5, maximum score (in price, the cheapest); 1, minimum score (in price, the most expensive).

(acrylonitrile butadiene) gloves provide protection against infection comparable to that offered by latex gloves [192] and similar permeability against cytotoxic agents [193]. For surgical procedures, synthetic polymers such as neoprene (polychloroprene), polyisoprene, butadiene, and elastiprene are recommended, given their biomechanical and barrier properties. However, their use is limited as they are expensive. Table 4 shows the different characteristics of rubber gloves (latex and synthetic) [194].

Avoidance of foods with cross-reactivity to latex

Patients with latex-fruit syndrome should be advised to avoid the fruits involved. No consensus has been reached on the avoidance of the 4 highest-risk foods, although no previous reactions to these foods have been reported, not even in the presence of subclinical sensitization or specific IgE against the main allergens causing this reactivity.

Specific Immunotherapy

Although considered an alternative, immunotherapy with latex has only been analyzed in 7 published studies using the parenteral or sublingual route [195-203]. All conclude that while the clinical sensitivity of patients can be reduced, the incidence of important adverse reactions is too high to recommend its habitual use, except under very controlled conditions and in very specific cases [203,204].

Prevention

Preventing latex allergy depends on the type of prevention chosen (primary or secondary), the clinical characteristics of the at-risk or sensitized individual, and the possibility of daily avoidance.

Current Regulations Regarding the Presence of Latex in Objects

General regulations

In Spain, health care products are regulated by Royal Decree 414/1996 of March 1, which transfers to the Spanish legal system Directive 93/42/EEC of June 14, 1993 concerning medical devices. Both European Union and Spanish regulations represent the legislation through which the conditions for the manufacture and commercialization of health care products are established.

Labeling

One of the most crucial needs for allergic patients is correct labeling of all latex products in order to facilitate immediate identification and thus enable the individual to avoid contact. In single-use medical gloves, provision of a label reading *Contains latex from natural rubber, which may cause allergic reactions* is regulated in UNE-EN 455-3. For other health care products a directive exists regarding the implications of the 93/42/EEC directive on sanitary products with regard to products containing natural latex.

As for the labeling of medications, a directive from the European Commission on Article 65 of the 2001/83/EC Directive contains warnings related to the presence of certain excipients in medications and makes information on the presence of latex and risks for allergic individuals mandatory. In Europe, the safety regulations on toys come under European Standard EN 71-1:1998 Safety of toys. Other latex products such as condoms, gloves for domestic use, and balls are not included in these regulations. In December 2001, the Spanish Safety Technical Commission of the National Consumer Institute issued a recommendation that the labels of all articles containing natural latex should carry suitable warnings. This recommendation is supported in Royal Decree 1468/1988 of December 2, which approved the labeling regulations, presentation, and advertising of industrial products sold directly to users with reference to the indication of the composition of the product.

Primary Prevention

Correctly validated protocols have been applied to prevent reactions to latex in children with spina bifida undergoing surgery. Application of these protocols has reduced the number of sensitized patients for the same number of operations [176,205-210]. No studies evaluate the efficacy of these measures in other at-risk populations [211-214]; however, it is advisable to implement them while data that support their implementation are being collected.

Surgery is not the only route of sensitization, as a considerable percentage of atopic children, who have never undergone surgery, are sensitized to latex [205,215]. Consequently, avoidance measures should be implemented not only in the hospital environment but also in primary care settings, dentist's offices, and any place in which at-risk children are attended.

In recent years, prevention strategies have been developed mainly in the health care setting. The complete substitution of sterile latex gloves with gloves made from other materials is controversial; however, even though complete substitution cannot be achieved, correct and rational use of latex gloves and alternatives that may be suitable for health care purposes should be promoted [68,216].

Furthermore, different scientific and health care sectors and users have promoted the use of gloves without latex. In 2002, the American Academy of Allergy, Asthma and Immunology published recommendations to avoid sensitization and development of latex allergy in health care settings [217], as follows: *(a)* rational use of latex; *(b)* use of nonsterile unpowdered gloves; and *(c)* in the case of sterile gloves, use of unpowdered gloves or, if they are powdered, use of those with a low protein content.

The Committee on Latex of the SEAIC subsequently published a document on rational use of gloves [217]. The basic recommendations of this document are to use gloves only when necessary, avoid powdered latex gloves, and always use synthetic gloves with allergic patients.

A systematic review from 2006 analyzed various aspects of latex allergy in health care workers [218]. Table 5 summarizes the main published studies on primary prevention programs in health care workers [219-226].

Table 5. Studies Assessing the Efficacy of Prevention Measures in Health Care Professionals

Author	Population	Prevention Strategy	Diagnostic Method	Efficacy Variable
Allmers et al (225)	Health care workers in Germany	Unpowdered gloves low in proteins	Questionnaire, skin test (challenges in some)	110 new cases/year (1997) 17 new cases/year (2001)
Saary et al (220)	School of Odontology N=131 (1995) N=97 (2000)	Unpowdered gloves low in proteins	Questionnaire, skin test (serum IgE in some)	Positive skin test: 10% (1995) 3% (2000)
Schimd et al (223)	School of Odontology N=226 (2000)	Unpowdered gloves low in proteins	Questionnaire, skin test (serum IgE in some)	New cases: 5.3% (1990) 1.3% (2000)
Hunt et al (221)	Health care workers (Mayo Clinic) N=12 000	Unpowdered gloves low in proteins	Questionnaire, skin test	Allergic patients: Incidence rate of 0.15% before 1993 0.027% after 1993
Tarlo et al (222)	Workers in 2 hospitals in Canada N=8000	Unpowdered gloves low in proteins	Questionnaire, skin test	Incidence: 25 cases/year (1994) 1 case /year (1999)

Abbreviation: Ig, immunoglobulin.

Secondary Prevention

In both sensitized and allergic patients, the most effective approach is avoidance; however, this is difficult, given the widespread presence of latex. Therefore, changes in the use of latex at home, school, and work and in the health care setting should be considered.

Secondary prevention in the health care worker

The use of unpowdered gloves and gloves with a low latex protein content leads to a reduction in the number of patients with symptoms and the concentrations of specific IgE [216,227-230]. Powdered gloves with low allergenicity lead to a significant reduction in hand eczema, thus allowing health care workers to remain in their posts [226,224]. As for reduction in the onset of symptoms, other studies seem to confirm the usefulness of latex avoidance measures, which also enable health care workers to continue to perform their work activities [230-266].

Secondary prevention in patients in the health care setting

Surgical operations are one of the most difficult issues to resolve, especially adequate preparation of operating rooms.

Several published protocols (mostly in nursing journals) advise different diagnostic and therapeutic procedures in latex-allergic patients [231-237].

Secondary prevention in patients outside the health care setting

Some authors have pointed out that it is impossible for patients to completely avoid latex in their daily lives, even though this would only be a real problem in a small group of highly sensitized patients prone to very severe reactions [238-241].

The quantity of information available is vast. In Spain, several patient associations, eg, the Spanish Association of Latex-Allergic Patients (Asociación Española de Alérgicos al Látex [http://www.alergialatex.es] and the Spanish Association of Food-Allergic and Latex-Allergic Patients (Asociación Española de Alérgicos a Alimentos y Látex [http://www.aepnaa.org]), provide information in Spanish. Scientific associations such as the Spanish Society of Allergology and Clinical Immunology (http://www.seaic.es) and the Scientific Society of Allergology and Clinical Immunology for Madrid and Castilla la Mancha (http://www.smclm.com) also provide information on the issue.

Despite the quantity of information available to latex-allergic patients, reactions are still reported sporadically. These are sometimes very severe, as a result of contact with latex as a hidden allergen in foods [72,113,242-244], toys, or other objects [245-247]. Such cases show the inefficiency of secondary prevention measures outside the health care setting [237-240].

Further studies are needed to broaden information on the efficacy of avoidance measures outside the health care setting, as well as their repercussion on quality of life [248].

Unresolved Issues

Despite research efforts, many important aspects of latex allergy have yet to be clarified. For example, greater

understanding of the natural progression of latex allergy in the general population would help to distinguish asymptomatic sensitization from real clinical allergy, interpret the different IgE responses to each of the allergenic latex proteins [249], establish the number of patients with asymptomatic sensitization who would develop symptomatic allergy [250-257,285-90], and decide on the appropriate follow-up for these patients. Increased knowledge would also help us to determine the clinical yield of preventive measures [258] and whether such measures should include avoidance of latex, especially when patients need to undergo medical or surgical procedures. Finally, the more data available, the more likely we are to know the complete range of risk factors for latex allergy [259]. In this context, a better understanding of the genetic polymorphisms associated with latex allergy would enable us to avoid latex exposure in allergic patients [260-264].

Another unresolved issue concerns allergy to plant foods whose allergens cross-react with latex [98,128]. We do not have precise and useful markers that enable us to identify which patients who are initially allergic to latex but not allergic to foods are at greatest risk of experiencing future allergic reactions when they come into contact with the foods in question.

We must also determine whether latex-allergic patients who follow a strict and prolonged avoidance regimen, especially in the workplace, and who achieve undetectable concentrations of specific IgE against latex, could overcome their illness and be considered cured. Similarly, the progression of patients who become allergic following early and continuous exposure to latex, such as those with spina bifida or those undergoing multiple operations, remains to be determined.

More high quality prospective studies are necessary to show whether prevention measures can really reduce the incidence of latex allergy in the workplace and the economic repercussions that this would have as regards sick leave and disabilities [15,73,219,224,258,265].

Specific immunotherapy must be further developed. Production of modified biotechnical allergens with lower allergenicity will likely reduce the number of adverse reactions [266-270].

The controversy surrounding the real risk of exposure to hard objects manufactured from rubber for latex-allergic individuals needs to resolved [271]. Many articles have been published of single cases or small groups of patients who have occasionally experienced reactions following exposure to these hard rubber objects, although such reports do not objectively demonstrate that the reaction was due to latex [272-278].

Finally, ways of identifying new at-risk groups need to be defined [279].

Key Points

- To date, 14 latex allergens have been identified.
- The incidence of latex allergy increases with the degree of exposure.
- The environmental concentrations of airborne latex allergens capable of sensitizing and producing symptoms are not well defined.
- It is possible to determine the amount of latex protein both in environmental air and on the surface of objects using immunoanalysis techniques and immunoblotting.
- All patients with suspected latex allergy should be referred to an allergologist for study.
- The clinical history is fundamental for diagnosis and should be completed with skin tests using the prick technique with appropriately validated extracts and occasionally also with the determination of specific IgE (against latex and recombinant allergens) and exposure tests.
- The natural progression of latex allergy in the general population is not well defined. It is best known in children with spina bifida or those undergoing multiple operations, although we are a long way from establishing a "route map for latex allergy".
- In occupational allergy to latex, sensitization appears to be proportional to the use of powdered latex gloves; consequently, replacement with unpowdered gloves or gloves containing no latex is recommended.
- Avoidance of reactions to latex involves educating patients and health care staff about latex allergy and the main sources of latex, paying special attention to soft rubber objects, and increasing knowledge of which plant foods may present clinical cross-reactivity with latex, especially banana, chestnut, avocado, and kiwi.
- In latex-allergic patients, associated allergy to foods must be ruled out, as must be latex allergy in patients allergic to specific fruits, especially banana, chestnut, avocado, and kiwi.
- All latex-allergic patients must be provided with a written report showing their diagnosis and setting out recommendations. Patients should carry a copy of the report with them at all times.
- Both patients and health care staff must know the different latex materials that can be used in medical and everyday settings that do not pose any risk for patients. Health centers must have action plans for latex-allergic patients.
- Indications for specific immunotherapy are limited. More clinical trials are required to define its clinical usefulness.
- Primary prevention protocols in children with spina bifida reduce the frequency of sensitization to latex; therefore, these children must avoid exposure to latex from birth. It would be advisable to apply this measure universally to other at-risk groups in the pediatric population.
- No published studies evaluate the efficacy of primary prevention programs in workers exposed to latex outside the health care setting.
- The use of unpowdered gloves and those with a low protein content lowers the incidence of latex allergy in health care workers and reduces the severity of symptoms in those who have already become sensitized. Few data are available from outside health care settings.
- Although it is not possible to achieve a completely latex-free health care environment, the use of avoidance protocols and substitution of latex materials will enable latex-allergic patients to safely undergo diagnostic and therapeutic procedures.

- As several aspects of this disease have yet to be clarified, further research should be encouraged.

References

1. Fahn A. Lacticifers in secreting tissues in plants. Acad Pres. London, New York, San Francisco, 1979; 223-43.
2. Quirce S, Conde Salazar L. Obtención y procesamiento del caucho natural. In: Alergia al Látex. Mra ediciones; 2002, p 13-25.
3. Vidal de Carcer M. Historia del Caucho. In: Tratado moderno de las industrias del caucho. Editor José Montesó. Barcelona y Buenos Aires, 1953. p 1-11.
4. Subramaniam A. The chemistry of natural rubber latex. In: Latex Allergy. Ed: Fink NJ. Immunol Allergy Clin N Am. 1995;15:1-21.
5. Walls RS. Latex allergy: a real problem. Med J Aust. 1996;164:707-8.
6. Blanco Guerra C, Quirce Gancedo S, De la Hoz Caballer B, Nieto García A, Tabar Purroy A. Reacciones de hipersensibilidad al látex del árbol del caucho. In: Tratado de Alergología. Editores Peláez, Dávila. Ergon 2007. p 1657-80.
7. Conde Salazar L, Miranda Romero A. Caucho y gomas: dermatosis por gomas y derivados. In: Dermatitis de contacto. JM Camarasa. Madrid Ed. Aula Medica 1999. p 225-36.
8. Stern G. Uberempfindlichkeit gegen Kaustchuck als Urasche von Urticaria und Quinckeschem Odem. Klin Wochenschrift. 1927;6:1096-7.
9. Nutter AF. Contact urticaria to rubber. Br J Dermatol. 1979;101:597-8.
10. Carrillo T, Cuevas M, Muñoz T, Hinojosa M, Moneo I. Contact urticaria and rhinitis from latex surgical gloves. Contact Dermatitis. 1986 Aug;15(2):69-72.
11. Barber Hernandez D, Lombardero Vega M. Composición alergénica del látex. In: Alergia a látex. Mra ediciones; 2002, p 13-25.
12. Thompson RL. Educational challenges of latex protein allergy. In: Fink J editor. Latex allergy. Philadelphia: Saunder. Immunol Allergy Clin North Am. 1995;15:159-74.
13. Leynadier F, Tran-Xuan T, Dry J. Allergenicity suppression in natural latex surgical gloves. Allergy. 1991;67:619-25.
14. 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 Aug;110(2):318-23.
15. Allmers H, Schmengler J, John SM. Decreasing incidence of occupational contact urticaria caused by natural rubber latex allergy in German health care workers. J Allergy Clin Immunol. 2004 Aug;114(2):347-51.
16. Yeang HY. Natural rubber latex allergens: new developments. Curr Opin Allergy Clin Immunol. 2004;4(2):99-104.
17. Rihs H-P, Raulf-Heimsoth M. Natural rubber latex allergens: Characterization and evaluation of their allergenic capacity. New Horizons, Pharmacia Diagnostics AB 2003; No 3.
18. Yeang HY, Cheong KF, Sunderasan E, Hamzah S, Chew NP, Hamid S, Hamilton RG, Cardosa MJ. The 14.6 kd rubber elongation factor (Hev b 1) and 24 kd (Hev b 3) rubber particle proteins are recognized by IgE from patients with spina bifida and latex allergy. J Allergy Clin Immunol. 1996;98(3):628-39.
19. Kurup VP, Yeang HY, Sussman GL, Bansal NK, Beezhold DH, Kelly KJ, Hoffman DR, Williams B, Fink JN. Detection of immunoglobulin antibodies in the sera of patients using purified latex allergens. Clin Exp Allergy. 2000;30:359-69.
20. Palosuo T, Lehto M, Kotovuori A, Kalkkinen N, Blanco C, Poza P, Carrillo T, Hamilton RG, Alenius H, Reunala T, Turjanmaa K. Latex allergy: low prevalence of immunoglobulin E to highly purified proteins Hev b 2 and Hev b 13. Clin Exp Allergy. 2007 Oct;37(10):1502-11.
21. Wagner B, Krebitz M, Buck D, Niggemann B, Yeang HY, Han KH, Scheiner O, Breiteneder H. Cloning, expression, and characterization of recombinant Hev b 3, a Hevea brasiliensis protein associated with latex allergy in patients with spina bifida. J Allergy Clin Immunol. 1999;104:1084-92.
22. Alenius H, Kalkkinen N, Lukka M, Turjanmaa K, Reunala T, Makinen- Kilujunen S, Yip E, Palosouto T. Purification and partial aminoacid sequencing of a 27-kDa natural rubber allergen recognized by latex-allergic children with spina bifida. Int Arch Allergy Immunol. 1995;106:258-62.
23. Bernstein DI, Biagini RE, Karnani R, Hamilton R, Murphy K, Bernstein C, Arif SA, Berendts B, Yeang HY. In vivo sensitization to purified Hevea brasiliensis proteins in health care workers sensitized to natural rubber latex. J Allergy Clin Immunol. 2003 Mar;111(3):610-6.
24. Slater JE, Vedvick T, Arthur-Smith A, Trybul DE, Kekwick RG. Identification, cloning, and sequence of a major allergen (Hev b 5) from natural rubber latex (Hevea brasiliensis). J Biol Chem. 1996 Oct 11;271(41):25394-9.
25. Lundberg M, Chen Z, Rihs HP, Wrangsjö K. Recombinant spiked allergen extract. Allergy. 2001 Aug;56(8):794-5.
26. Beezhold DH, Hickey VL, Slater JE, Sussman GL. Human IgE-binding epitopes of the latex allergen Hev b 5. J Allergy Clin Immunol. 1999 Jun;103(6):1166-72.
27. Blanco C, Diaz-Perales A, Collada C, Sánchez-Monge R, Aragoncillo C, Castillo R, Ortega N, Alvarez M, Carrillo T, Salcedo G. Class I chitinases as potential panallergens involved in the latex-fruit syndrome. J Allergy Clin Immunol. 1999 Mar;103(3 Pt 1):507-13.
28. Yeang HY. Prevalence of latex allergy may be vastly overestimated when determined by in vitro assays. Ann Allergy Asthma Immunol. 2001 Aug;87(2):164-5.
29. Wagner S, Breiteneder H, Simon-Nobbe B, Susani M, Krebitz M, Niggemann B, Brehler R, Scheiner O, Hoffmann-Sommergruber K. Hev b 9, an enolase and a new cross-reactive allergen from hevea latex and molds. Purification, characterization, cloning and expression. Eur J Biochem. 2000 Dec;267(24):7006-14.
30. Rihs HP, Chen Z, Rozynek P, Cremer R. Allergenicity of rHev b 10 (manganese-superoxide dismutase). Allergy. 2001 Jan;56(1):85-6.
31. Rihs HP, Ruëff F, Lundberg M, Rozynek P, Barber D, Scheurer S, Cisteró-Bahima A, Brüning T, Raulf-Heimsoth M. Relevance of the recombinant lipid transfer protein of Hevea brasiliensis: IgE-binding reactivity in fruit-allergic adults. Ann Allergy Asthma Immunol. 2006 Nov;97(5):643-9.
32. D'Amato A, Bachi A, fasoli E, Boschetti E, Peltre G, Senechal H, Sutra JP, Citterio A, Righetti PG. In-depth exploration of Hevea brasiliensis latex proteome and "hidden allergens" via combinatorial peptide ligand libraries. J Proteomics. 2010;73(7):13-80.

33. Lee MF, Chen YH, Lin HC, Wang HL, Hwang GY, Wu Ch. Identification of Hevamine and Hev b 1 as major latex allergens in Taiwan. Int Arch Allergy Immunol. 2005;139(1):38-44
34. Swanson MC, Bubak ME, Hunt LW, Yunginger JW, Warner MA, Reed CE. Quantification of occupational latex aeroallergens in a medical center. J Allergy Clin Immunol. 1994;94:445-51.
35. Sussman GL, Liss GM, Deal K, Brown S, Cividino M, Siu S, Beezhold DH, Smith G, Swanson MC, Yunginger J, Douglas A, Holness DL, Lebert P, Keith P, Waserman S, Turjanmaa K. Incidence of latex sensitization among latex glove users. J Allergy Clin Immunol. 1998 Feb;101(2 Pt 1):171-8.
36. Baur X, Chen Z, Allmers H. Can a threshold limit value for natural rubber latex airborne allergens be defined? J Allergy Clin Immunol. 1998;101:24-7.
37. Charous BL, Schuenemann PJ, Swanson MC. Passive dispersion of latex aeroallergen in a healthcare facility. Ann Allergy Asthma Immunol. 2000;85:285-90.
38. Tarlo SM, Sussman G, Contala A, Swanson MC. Control of airborne latex by use of powder free latex gloves. J Allergy Clin Immunol. 1994;93:985-9.
39. Swanson M, Yunginger J, Reed C. Immunochemical characterization of airborne natural rubber latex allergen in medical and dental office buildings, Healthy Buildings '95 International Conference, Milan, 1995. Vol. 9.
40. Heilman DK, Jones RT, Swanson M, Yunginger JW. A prospective, controlled study showing that rubber gloves are the major contributor to latex aeroallergen levels in the operating room. J Allergy Clin Immunol. 1996;98:325-30.
41. Allmers H, Brehler R, Chen Z, Raulf-Heimsoth M, Fels H, Baur X. Reduction of latex aeroallergens and latex-specific IgE antibodies in sensitized workers after removal of powdered natural rubber latex gloves in a hospital. J Allergy Clin Immunol. 1998;102:841-6.
42. Swanson M, Yunginger J, Lam V, Truscott W. Airborne natural rubber allergen concentrations within a Malaysian latex glove production facility. In: Indoor Air '99, Proceedings of the 8th International Conference on Indoor Quality and Climate-Indoor Air '99, Edinburgh, 1999. Vol. 1.
43. Swanson M, Zakharov S, Luss L, Babakhin A, Dubuske L. Latex aeroallergen quantification in hospitals of Moscow, Russia. Ann Allergy Asthma Immunol. 2001;87:307-10.
44. Williams PB, Buhr MP, Weber RW, Volz MA, Koepke JW, Selner JC. Latex allergen in respirable particulate air pollution. J Allergy Clin Immunol. 1995;95:88-95.
45. Miguel AG, Cass GR, Weiss J, Glovsky MM. Latex allergens in tire dust and airborne particles. Environ Health Perspect. 1996;104:1180-6.
46. Quirce S, Escudero C, Swanson MC, Martínez-Aramayona MJ, Fernández-Nieto M, Sastre J. Latex aeroallergen concentrations in ambulances. J Allergy Clin Immunol. 2004;114:978-9.
47. Namork E, Kurup VP, Aasvang GM, Johansen BV. Detection of latex allergens by immunoelectron microscopy in ambient air (PM10) in Oslo, Norway (1997-2003). J Environ Health. 2004;67:20-6.
48. Namork E, Johansen BV, Løvik M. Detection of allergens adsorbed to ambient air particles collected in four European cities. Toxicol Lett. 2006;165:71-8.
49. Crippa M, Belleri L, Mistrello G, Tedoldi C, Alessio l. Prevention of latex allergy among health care workers and in the general population: latex protein content in devices commonly used in hospitals and general practice. Int Arch Occup Environ Health. 2006:79:550-7.
50. Reiter JE. Latex sensitivity: An industrial hygiene perspective. J Allergy Clin Immunol. 2002;110:S121-8.
51. Yassin M, Lierl M, Fischer T, O'Brien K, Cross J, Steinmetz C. Latex allergy in Hospital employees. Ann Allergy. 1994;72:245-9.
52. Moneret-Vautrin DA, Beaudouin E, Widmer S, Mouton C, Kanny G, Prestat F, Kohler C, Feldmann L. Prospective study of risk factors in natural rubber latex hypersensitivity. J Allergy Clin Immunol. 1993 Nov;92(5):668-77.
53. Archambault S, Malo JL, Infante-Rivard C, Ghezzo H, Gautrin D. Incidence of sensitization, symptoms and probable occupational rhinoconjunctivitis and asthma in apprentices starting exposure to latex. J Allergy Clin Immunol. 2001;107:921-3.
54. McCormack B, Cameron M, Biel L. Latex sensitivity: an occupational health strategic plan. AAOHN J. 1995:43:190-6.
55. Korniewicz DM, Kelly KJ. Barrier protection and latex allergy associated with surgical gloves. AORN J. 1995;61:1037-44.
56. Tomazic VJ, Shampaine EL, Lamanna A, Withrow TJ, Adkinson NF Jr, Hamilton RG. Cornstarch powder on latex products is an allergen carrier. J Allergy Clin Immunol. 1994;93:751-8.
57. De la Hoz B. Estrategias para la prevención de la alergia al látex. In: Blanco Guerra C, Quirce Gancedo S. Alergia al látex. Barcelona, MRA ediciones; 2002:213-44.
58. UNE-EN-455-3 Guantes médicos para un solo uso, parte 3: requisitos y ensayos para la evaluación biológica. Junio 2000.
59. Baur X, Chen Z, Raulf-heimsoth M, Degens P. Protein and allergen content of various natural latex articles. Allergy. 1997;52:661-4.
60. Beezhold D, Bradley P, Liss G, Sussman G. Correlation of protein levels with skin prick test reactions in patients allergic to latex. J Allergy Clin Immunol. 1996;98:1097-102.
61. Palosuo T, Mäkinen-Kiljunen S, Alenius H, Reunala T, Yip E, Turjanmaa K. Measurement of natural rubber latex allergen levels in medical gloves by allergen-specific IgE-ELISA inhibition, RAST-inhibition, and skin prick test. Allergy. 1998;53:59-67.
62. Yip E, Turjanmaa K, Ng PH, Mok KL. Allergic responses and levels of extractable proteins in NR latex gloves and dry rubber products. J Nat Rubber Res. 1994;9:79-86.
63. Levy DA, Allouache S, Chabane MH, Leynadier F. Power-free protein-poor natural rubber latex gloves and latex sensitization. JAMA. 1999;281:988-9.
64. Brown RH, Taenkhum K, Buckley TJ, Hamilton RG. Different latex aeroallergen size distributions between powdered surgical and examination gloves: significance for environmental avoidance. J Allergy Clin Immunol. 2004;114:358-63.
65. Hinojosa M. La prevención en el asma ocupacional. Rev esp Alergol Inmunol Clin. 1997;12:211-7.
66. Reed CE, Swanson MC, Li JT. Environmental monitoring of protein aeroallergens. In: Bernstein IL, Chan-Yeung M, Maco JL, Bernstein DI, editors. Asthma in the workplace. New York: Marcel-Dekker,Inc; 1999. p. 249-75.
67. Poulus LM, O'Meara TJ, Hamilton RG, Tovey ER. Inhaled latex allergen (Hev b 1). J Allergy Clin Immunol. 2002;109:701-6.

68. Warshaw HM. Latex allergy. J A Acad Dermatol. 1998;39:1-24.
69. Jaeger D, Kleinhans D, Czuppon AB, Bauer X. Latex-specific proteins causing immediate-type cutaneous, nasal, bronchial, and systemic reactions. J Allergy Clin Immunol. 1992;9:501-7.
70. Diéguez MC, Pulido Z, de la Hoz B, Blanco R, Cerecedo I, Fernández-Caldas E, Swanson M. Latex allergy in healthcare workers: An epidemiological study in a Spanish hospital. Allergy Asthma Proc. 2007;28(5):564-70.
71. Lagier F, Vervloet D, Lhermet I, Poyen D, Charpin D. Prevalence of latex allergy in operating room nurses. J Allergy Clin Immunol. 1992;90:319-22.
72. Mak RK, O'Gorman-Lalor O, Croom A, Wakelin SH. An unusual case of latex allergy: contact urticaria from natural rubber latex in chocolate bar wrappers. Clin Exp Dermatol. 2005;30(2):190-1.
73. Filon FL, Radman G. Latex allergy: a follow up study of 1040 healthcare workers. Occup Environ Med. 2006;63(2):121-5.
74. Doutre.MS. Occupational contact urticaria and protein contact dermatitis Eur J Dermatol. 2005;15(6):419-24.
75. Lleonart R, Corominas M. Rinitis ocupacional en una fábrica de esquíes. Alergol Inmunol Clin. 2005;20(ext 2):142.
76. Vandenplas O. Occupational asthma caused by natural rubber latex. Eur Respir J. 1995;8:1957-65.
77. Ho A, Chan H, Tse KS, Chan-Yeung M. Occupational asthma due to latex in health care workers. Thorax. 1996;51:1280-2.
78. Acero S, Alvarez MJ, García BE, Echechipía S, Olaguibel JM, Tabar AI. Occupational asthma from natural rubber latex. Specific inhalation challenge test and evolution. J Investig Allergol Clin Immunol. 2003;13:155-61.
79. Turjanmaa K. Incidence of immediate allergy to latex gloves in hospital personnel. Contact Dermatitis. 1987;17:270-5.
80. Garabrant DH, Roth HD, Parsad R, Ying GS, Weiss J. Latex sensitization in health care workers and in the US General Population. Am J Epidemiol. 2001;153:515-22.
81. Gautrin D, Ghezzo H, Infante-Rivard C, Malo JL. Incidence and determinants of IgE-mediated sensitization in apprentices. A prospective study. Am J Respir Crit Care Med. 2000;162:1222-8.
82. Salkie ML. The prevalence of atopy and hypersensitivity to latex in medical laboratory technologists. Arch Pathol Lab Med. 1993;117:897-9.
83. Watts DN, Jacobs RR, Forrester B, Bartolucci A. An evaluation of the prevalence of latex sensitivity among atopic and non-atopic intensive care workers. Am J Ind Med. 1998;34:359-63.
84. Sri-akajunt N, Sadhra S, Burge PS. Latex sensitisation amongst workers in Thai rubber estates and latex glove factories. Rev fr Allergology. 1997;37:1217.
85. Baur X, Jäger D. Airborne antigens from latex gloves [letter]. Lancet. 1990;335:912.
86. Marcos C, Lázaro M, Fraj J, Quirce S, de la Hoz B, Fernández-Rivas M, Losada E. Occupational asthma due to latex surgical gloves. Ann Allergy. 1991;67:319-23.
87. Bubak ME, Reed CE, Fransway AF, Yunginger JW, Jones RT, Carlson CA, Hunt LW. Allergic reactions to latex among health-care workers. Mayo Clin Proc. 1992 Nov;67(11):1075-9.
88. Tarlo SM, Wong L, Roos J, Booth N. Occupational asthma caused by latex in a surgical glove manufacturing plant. J Allergy Clin Immunol. 1990;85:626-31.
89. Vandenplas O, Delwiche JP, Evrard G, Aimont P, van der Brempt X, Jamart J, Delaunois L. Prevalence of occupational asthma due to latex among hospital personnel. Am J Respir Crit Care Med. 1995 Jan;151(1):54-60.
90. Pisati G, Baruffini A, Bernabeo F, Falagiani P. Environmental and clinical study of latex allergy in a textile factory. J Allergy Clin Immunol. 1998;101:327-9.
91. Lopata AL, Adams S, Kirstein F, Henwood N, Raulf-Heimsoth M, Jeebhay MF. Occupational allergy to latex among loom tuners in a textile factory. Int Arch Allergy Immunol. 2007;144:64-8.
92. Weytjens K, Labrecque M, Malo JL, Cartier A. Asthma to latex in a seamstress. Allergy. 1999;54:287-96.
93. Martínez Rivera C, Monso Molas E, Izquierdo Ramírez J, Morera Prats J. Latex occupational asthma in the production of chewing gum. A case report. Med Clin. 1998;111:399.
94. Orfan NA, Reed R, Dykewics MS, Ganz M, Kolski GB. Occupational asthma in a latex doll manufacturing plant. J Allergy Clin Immunol. 1994;94:826-30.
95. Van der Walle H, Brunsveld V. Latex allergy among hairdressers. Contact Dermatitis. 1995;32:177.
96. Sussman GL, Lem D, Liss G, Beezhold D. Latex allergy in housekeeping personnel. Ann Allergy Asthma Immunol. 1995 May;74(5):415-8.
97. Carrillo T, Blanco C, Quiralte J, Castillo R, Cuevas M, Rodríguez de Castro F. Prevalence of latex allergy among greenhouse workers. J Allergy Clin Immunol. 1995;90:319-22.
98. Turjanmaa K, Makinen-Kiljunen S, Reunala T, Alenius H, Palosuo T. Natural rubber latex allergy - the European experience. Immunol Allergy Clin North Am. 1995;15:71-88.
99. Quirce S, Fernández-Nieto M, de Miguel J, Sastre J. Chronic cough due to latex-induced eosinophilic bronchitis. J Allergy Clin Immunol. 2001;108:143.
100. Laxenaire MC, Mertes PM; Groupe d'Etudes des Réactions Anaphylactoïdes Peranesthésiques. Anaphylaxis during anaesthesia. Results of a two-year survey in France. Br J Anaesth. 2001 Oct;87(4):549-58.
101. Mertes PM, Laxenaire MC; GERAPAnaphylactic and anaphylactoid reactions occurring during anaesthesia in France. Seventh epidemiologic survey (January 2001-December 2002). Ann Fr Anesth Reanim. 2004;23(12):1133-43.
102. Mertes PM, Alla F. Laxenaire MC. Anaphylactic and anaphylactoid reactions occurring during anesthesia in France in 1999-2000. Anesthesiology. 2003;99:536-45.
103. Sánchez-Ródenas L, Sánchez-Ortega JL. Intraoperative anaphylaxis in a patient with undiagnosed latex sensitivity. Rev Esp Anestesiol Reanim. 2005;52(2):67-70.
104. Thong BY, Yeow-Chan. Anaphylaxis during surgical and interventional procedures. Ann Allergy Asthma Immunol. 2004;92(6):619-28.
105. Karila C, Brunet-Langot D, Labbez F, Jacqmarcq O, Ponvert C, Paupe J, Scheinmann P, de Blic J. Anaphylaxis during anesthesia: results of a 12-year survey at a French pediatric center. Allergy. 2005;60(6):828-34.
106. Lieberman P. Anaphylactic reactions during surgical and medical procedures. J Allergy Clin Immunol. 2002;110(2 Suppl):S64-9.
107. Draisci G, Nucera E, Pollastrini E, Forte E, Zanfini B, Pinto R, Patriarca G, Schiavino D, Pietrini D. Anaphylactic reactions during cesarean section. Int J Obstet Anesth. 2007;16(1):63-7.
108. Ogata J, Minami K. Synthetic oxytocin and latex allergy. Br J Anaesth. 2007;98(6):845-6.

109. Ownby DR, Tomlanovich M, Sammons N, McCullough J. Anaphylaxis associated with latex allergy during barium enema examinations. Am J Roentgenol. 1991;156:903-8.
110. Gelfand DW. Barium enemas, latex balloons, and anaphylactic reactions. Am J Roentgenol. 1991;156(1):1-2.
111. Spears FD, Liu DW. Anaphylactoid reaction to syntocinon? Anaesthesia. 1994;49:550-1.
112. Beezhold D, Reschke J, Kostyal D. Latex Protein: a "hidden" food allergen? Allergy and Asthma Proc. 2000;21:301-6.
113. Bernardini R, Novembre E, Lombardi E, Pucci N, Vierucci A. Anaphylaxis to latex after ingestion of a cream-filled dougnhut contaminated with latex. J Allergy Clin Immunol. 2002;110:534-5.
114. http://www.aesan.msc.es/aesa/web/AESA.jsp
115. Blanco C, Carrillo T, Castillo R, Quiralte J, Cuevas M. Latex allergy: clinical features and cross reactivity with fruits. Ann Allergy. 1994;73:309-14.
116. Lavaud F, Prevost A, Cossart C, Guerin L, Bernard J, Kochman S. Allergy to latex, avocado pear, and banana: evidence for a 30 kD antigen in immunoblotting. J Allergy Clin Immunol. 1995;95:557-64.
117. Delbourg MF, Guilloux L, Moneret-Vautrin DA, Ville G. Hypersensitivity to banana in latex-allergic patients. Identification of two major banana allergens of 33 and 37 kD. Ann Allergy Asthma Immunol. 1996;76:321-6.
118. Beezhold DH, Sussman GL, Liss GM, Chang NS. Latex allergy can induce clinical reactions to specific foods. Clin Exp Allergy. 1996;26:416-22.
119. Brehler R, Theissen U, Mohr C, Luger T. "Latex-fruit syndrome": frequency of cross-reacting IgE antibodies. Allergy. 1997;52:404-10.
120. Kim KT, Hussain H. Prevalence of food allergy in 137 patients. Allergy Asthma Proc. 1999;20:95-7.
121. Mäkinen-Kiljunen S. Banana allergy in patients with immediate-type hypersensitivity to natural rubber latex: characterization of cross-reacting antibodies and allergens. J Allergy Clin Immunol. 1994;3:990-6.
122. M'Raihi L, Charpin D, Pons A, Bougrand P, Vervloet D. Cross-reactivity between latex and banana. J Allergy Clin Immunol. 1991;87:129-30.
123. Rodríguez M, Vega F, García MT, Panizo C, Laffond E, Montalvo A, Cuevas M. Hypersensitivity to latex, chestnut, and banana. Ann Allergy. 1993;70:31-4.
124. Fernández de Corres L, Moneo I, Muñoz D, Bernaola G, Fernández E, Audicana M, Urrutia I. Sensitization from chestnuts and bananas in patients with urticaria and anaphylaxis from contact with latex. Ann Allergy. 1993;70:35-9.
125. Añíbarro B, García-Ara MC, Pascual C. Associated sensitization to latex and chestnut. Allergy. 1993;70:130-1.
126. Carriles Hulett A, Sanchez Borges M, Von Scanzoni C, Medina Jr. Very low frecuency of latex and fruti allergy in patients with spina bifida from Venezuela: influence of socioeconomic factors. Ann Allergy Asthma Immunol. 1995;75:62-4.
127. Blanco C, Carrillo T, Castillo R, Quiralte J, Cuevas M. Avocado hypersensitivity. Allergy. 1994;49:454-9.
128. Blanco C. Latex-fruit syndrome. Curr Allergy Asthma Rep. 2003;3:47-53.
129. Wagner S, Radauer C, Hafner C, Fuchs H, Jensen-Jarolim E, Wüthrich B, Scheiner O, Breiteneder H. Characterization of cross-reactive bell pepper allergens involved in the latex-fruit syndrome. Clin Exp Allergy. 2004;34:1739-46.
130. Karisola P, Kotovuori A, Poikonen S, Niskanen E, Kalkkinen N, Turjanmaa K, Palosuo T, Reunala T, Alenius H, Kulomaa MS. Isolated hevein-like domains, but not 31-kd endochitinases, are responsible for IgE-mediated in vitro and in vivo reactions in latex-fruit syndrome. J Allergy Clin Immunol. 2005;115(3);598-605.
131. Yassin MS, Sanyurah S, Lierl MB, Fischer TJ, Oppenheimer S, Cross J, O'Brien K, Steinmetz C, Khoury J. Evaluation of latex allergy in patients with meningomyelocele. Ann Allergy. 1992;69:207-11.
132. Eseverri Jl, Botey J, Cozzo M, Pena M, Marín AM. Prevalence of allergy to latex in the pediatric population. Allergol Immunopathol. 1999;27:133-40.
133. Niggemann B, Buck D, Michael T, Wahn U. Latex provocation tests in patients with spina bifida: who is at risk of becoming symptomatic? J Allergy Clin Immunol. 1998;102:665-70.
134. Nieto A, Estornell F, Mazón A, Reig C, García Ibarra F. Allergy to latex in spina bifida: a multivariate study of associated factors in 100 consecutive patients. J Allergy Clin Immunol. 1996;98:501-7.
135. Michael T, Niggemann B, Mores A, Seidel U, Wahn U, Scheffner D. Risk factors for latex allergy in patients with spina bifida. Clin Exp Allergy. 1996;26:934-9.
136. Kelly KJ, Pearson ML, Kurup VP, Havens PL, Byrd RS, Setlock MA, Butler JC, Slater JE, Grammer LC, Resnick A, Roberts M, Jarvis MR, Davis JP, Fink NJ. 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.
137. Bode CP, Füllers U, Röseler S, Wawer A, Bachert C, Wahn U. Risk factors for latex hypersensitivity in childhood. Pediatr Allergy Immunol. 1996;7:157-63.
138. De Swert LF, Van Laer KM, Verpoorten CM, Van Hoeyveld EM, Cadot P, Stevens EA. Determination of independent risk factors and comparative analysis of diagnostic methods for immediate type latex allergy in spina bifida patients. Clin Exp Allergy. 1997 Sep;27(9):1067-76.
139. Mazón A, Nieto A, Estornell F, Reig C, García Ibarra F. Factors that influence the presence of symptoms caused by latex allergy in children with spina bifida. J Allergy Clin Immunol. 1997;99:600-4.
140. Pamiés R, Oliver F, Raulf-Heimsoth M, Rihs HP, Barber D, Boquete M, Nieto A, Mazón A. et al. Patterns of latex allergen recognition in children sensitised to natural rubber latex. Pediatr Allergy Immunol. 2006 Feb;17(1):55-9.
141. Pridgeon C, Wild G, Asworth F, Egner W, Ward AM. Assessment of latex allergy in a healthcare population: are the available tests valid? Clin Exp Allergy. 2000;30:1444-9.
142. Nettis E, Dambra P, Soccio AL, Ferrannini A, Tursi A. Latex hypersensitivity: relationship with positive prick test and patch test responses among hairdressers. Allergy. 2003;58:57-61.
143. Hamilton RG, Adkinson NF. Diagnosis of natural rubber latex allergy: multicenter latex skin testing efficacy study. Multicenter Latex Skin Testing Study Task Force. J Allergy Clin Immunol. 1998;102:482-90.
144. Brown RH, Schauble JF, Hamilton RG. Prevalence of latex allergy among anaesthesiologists: identification of sensitized but asymptomatic individuals. Anaesthesiology. 1998;89:292-9.

145. Woods JA, Lambert S, Platts-Mills TA, Drake DB, Edlich RF. Natural rubber latex allergy: spectrum, diagnostic approach and therapy. J Emerg Med. 1997;15:71-85.
146. Beuers U, Baur X, Schraudolph M, Richter WO. Anaphylactic shock after game of squash in atopic woman with latex allergy. Lancet. 1990:335:1095.
147. Garabrant DH, Schweitzer S. Epidemiology of latex sensitization and allergies in health care workers. J Allergy Clin Immunol. 2002;110(2 Suppl):S82-95.
148. Nieto A, Mazón A, Estornell F, Reig C, García Ibarra F. The search of latex sensitization in spina bifida: diagnostic approach. Clin Exp Allergy. 2000;30:264-9.
149. Blanco C, García Dumpiérrez A, Almeida Quintana L. Utilidad y limitaciones en las técnicas diagnósticas. In: Blanco Guerra C, Quince Cancedo S. Alergia al látex. Barcelona. MRA ediciones. 2002;6:101-19.
150. Rose RF, Lyons P, Horne H, Mark Wilkinson S. A review of the materials and allergens in protective gloves. Contact Dermatitis. 2009 Sep;61(3):129-37.
151. Turjanmaa K, Palosuo T, Alenius H, Leynadier F, Autegarden JE, André C, Sicard H, Hrabina M, Tran TX. Latex allergy diagnosis: in vivo and in vitro standardization of a natural rubber latex extract. Allergy. 1997 Jan;52(1):41-50.-2.
152. Lombardero M, Barber D, Rico P, Wikborg T, Sastre J. Characterization of latex extract for clinical use. In vitro measurements. J Allergy Clin Immunol. 2000;105:261
153. AAACI Position Statement: The use of Standardized Allergen Extracts. From the Committee on Allergen Standardization. 1997. www.aaaai.org
154. Nicolaou N, Johnston GA. Anaphylaxis following prick testing with natural rubber latex. Contact Dermatitis. 2002;47(4):251-2.
155. Rietschel RL, Fowler JF. Allergy to rubber. In: Fisher's Contact Dermatitis. 5th ed. Philadelphia. Lippincott Williams & Wilkins 2001; 31:533-560.
156. Wakelin SH, Jenkins RE, Rycroft RJ, McFadden JP, White IR. Patch testing with natural rubber latex. Contact Dermatitis. 1999 Feb;40(2):89-93.
157. Wilkinson SM, Beck MH. Allergic contact dermatitis from latex rubber. Br J Dermatol. 1996 May;134(5):910-4.
158. Bendewald MJ, Farmer SA, Davis MD. An 8-year retrospective review of patch testing with rubber allergens: the Mayo Clinic experience. Dermatitis. 2010 Feb;21(1):33-40.
159. Lezaun A, Marcos C, Martín JA, Quirce S, Díez Gómez ML. Contact dermatitis from natural latex. Contact Dermatitis. 1992 Nov;27(5):334-5.
160. Wyss M, Elsner P, Wüthrich B, Burg G. Allergic contact dermatitis from natural latex without contact urticaria. Contact Dermatitis. 1993 Mar;28(3):154-6.
161. Blanco C, Carrillo T, Ortega N, Alvárez M, Domínguez C, Castillo R. Comparison of skin-prick test and specific serum IgE determination for the diagnosis of latex allergy. Clin Exp Allergy. 1998;28:971-6.
162. Steinman H, Ruden S. Latex allergen components. In: ImmunoCAP. Native and recombinant allergen components. Uppsala. X-O Graf Tryckeri. 2006:41-58.
163. Kelly KJ, Kurup V, Zachadsen M, Resnick A, Fink JN. Skin and serologic testing in diagnosis of latex allergy. J Allergy Clin Immunol. 1993;91:1140-5.
164. Kurup VP, Kelly KJ, Turjanmaa K, Alenius H, Reunala T, Palouso T, Fink JN. Immunoglobulin E reactivity to latex antigens in the sera of patients from Finland and the United States. J Allergy Clin Immunol. 1993;91:1128-34.
165. Ownby DR, Magera B, Williams PB. A blinded multi-center evaluation of two commercial in vitro tests for latex-specific IgE antibodies. Ann Allergy Asthma Immunol. 2000;84:193-6.
166. Ebo DG, Stevens WJ, Bridts CH, De Clerck LS. Latex-specific IgE, skin testing and lymphocyte transformation to latex in latex allergy. J Allergy Clin Immunol. 1997;100:618-23.
167. Ylitalo L, Alenius H, Turjanmaa K, Palouso T, Reunala T. IgE antibodies to prohevein, hevein and rubber elongation factor in children with latex allergy. J Allergy Clin Immunol. 1998;102:659-64.
168. Gruber C, Buck D, Wahn U, Niggemann B. Is there a role for immunoblots in the diagnosis of latex allergy? Intermethod comparison of in vitro and in vivo IgE assays in spina bifida patients. Allergy. 2000;55:476-83.
169. Domínguez Ortega J, Domínguez Ortega C. Actualización de las aplicaciones de la citometría de flujo en el diagnóstico de las enfermedades alérgicas. Alergol Inmunol Clin. 2004;19:233-43.
170. Sanz ML, Gamboa PM, García-Avilés C, Vila L, Diéguez I, Antépara I, De Weck AL. Flow-cytometric cellular allergen stimulation test in latex allergy. Int Arch Allergy Immunol. 2003;130:33-9.
171. Sanz ML, García-Avilés MC, Tabar AI, Anda M, García BE, Barber D, Salcedo G, Rihs HP, Raulf-Heimsoth M. Basophil Activation Test and specific IgE measurements using a panel of recombinant natural rubber latex allergens to determine the latex allergen sensitization profile in children. Pediatr Allergy Immunol. 2006;17:148-56.
172. Ebo DG, Lechkar B, Schuerwegh AJ, Bridts CH, De Clerck LS, Stevens WJ. Validation of a two-color flow cytometric assay detecting in vitro basophil activation for the diagnosis of IgE-mediated natural rubber latex allergy. Allergy. 2002;57:706-12.
173. Hemery ML, Arnoux B, Dhivert-Donnadieu H, Rongier M, Barbotte E, Verdier R, Demoly P. Confirmation of the diagnosis of natural rubber latex allergy by the Basotest method. Int Arch Allergy Immunol. 2005;136:53-7.
174. Turjanmaa K, Reunala T, Rasanen L. Comparison of diagnostic methods in latex surgical glove contact urticaria. Contact Dermatitis. 1988;19:241-7.
175. Hamilton RG, Adkinson NF. Validation of the latex glove provocation procedure in latex-allergic subjects. Ann Allergy Asthma Immunol. 1997;79:266-72.
176. Niggemann B, Breiteneder H. Latex allergy in children. Int Arch Allergy Immunol. 2000;121:98-107.
177. Quirce S, Swanson MC, Fernández-Nieto M, de las Heras M, Cuesta J, Sastre J. Quantified environmental challenge with absorbable dusting powder aerosol from natural rubber latex gloves. J Allergy Clin Immunol. 2003;111:788-94.
178. Vandeplas O, Binard-Van Cangh F, Brumagne A, Caroyer JM. Occupational asthma in symptomatic workers exposed to natural rubber latex: evaluation of diagnostic procedures. J Allergy Clin Immunol. 2001;107:542-7.
179. Kurtz KM, Hamilton RG, Schaefer JA, Adkinson NF. A hooded exposure chamber method for semiquantitative latex aeroallergen challenge. J Allergy Clin Immunol. 2001;107:178-84.

180. Laoprasert N, Swanson MC, Jones RT, Schroeder DR, Yunginger JW. Inhalation challenge testing of latex-sensitive health care workers and the effectiveness of laminar flow HEPA-filtered helmets in reducing rhinoconjunctival and asthmatic reactions. J Allergy Clin Immunol. 1998;102:998-1004.
181. Aragoneses E, de la Hoz, Lizarza S. Special bronquial challenge in occupational asthma caused by latex [Abstract]. J Allergy Clin Immunol. 1999;103:S618.
182. Quirce Cancedo S, Olaguibel Rivera JM. Asma causada por látex. In: Blanco Guerra C, Quince Cancedo S. Alergia al látex. Barcelona. MRA ediciones. 2002;7:123-45.
183. Palczynski C, Walusiak J, Ruta A, Gorski P. Occupational allergy to latex: Life-threatening reactions in health care workers. Report of three cases. Int J Occup Med Environ Health. 1997;10:297-301.
184. Kari O, Lauerma H, Alenius H, Pauloso T, Reunala T. Ocular challenge with natural rubber latex. J Allergy Clin Immunol. 1997;99:343.
185. Palczynski C, Walusiak J, Ruta A, Gorski P. Nasal provocation test in the diagnosis of natural rubber latex allergy. Allergy. 2000;55:34-41.
186. Poley GE, Slater JE. Latex allergy. J Allergy Clin Immunol. 2000;105:1054-62.
187. Alenius H, Turjanmaa K, Palosuo T. Natural rubber latex allergy. Occup Environ Med. 2002;59:419-24.
188. Valls A, Pascual CY, Caballero MT, Martín Esteban M. Alergia al látex. Allergol Immunolpathol. 2004;32:295-305.
189. Cullinan P, Brown R, Field A, Houriahne J, Jones M, Kekwick R, Rycroft R, Stenz R, Williams S, Woodhouse C. Latex allergy. A position paper of the British Society of Allergy and Clinical Immunology. Clin Exp Allergy. 2003;33:1484-99.
190. Korniewicz DM. Barrier protection of latex. Immunol Allergol Clin North Am. 2005;15:123-37.
191. Douglas A, Simon T, Goddard M. Barrier durability of latex and vinyl medical gloves in clinical settings. Am Ind Hyg Assoc J. 1997;58:672-6.
192. Rego A, Roley L. In-use barrier integrity of gloves: latex and nitrile superior to vinyl. Am J Infect Control. 1999;27:405-10.
193. Wallemacq PE, Capron A, Vanbinst R, Boeckmans E, Gillard J, Favier B. Permeability of 13 different gloves to 13 cytotoxic agents under controlled dynamic conditions. Am J Health Syst Pharm. 2006;63:547-56.
194. Lleonart R, Rubira NM. Prevención de la alergia al látex en el personal sanitario. J Investig Allergol Clin Immunol. 2006;2:85-8.
195. Toci G, Shah S, Al-Faqih A, Beezold D, McGeady SJ. Oral Latex Desensitization of Healthcare Workers. J. Allergy Clin Immunol. 2001;101:1:2:S161.
196. Pereira C, Rico P, Lourenço M, Lombardero M, Pinto-Mendes J, Chieira J. Specific immunotherapy for occupational latex allergy. Allergy. 1999;54:291-3.
197. Nucera E, Schiavino D, Buonomo A, Roncallo C, Del Ninno M, Milani A, Pollastrini E, Patriarca G. Latex rush desensitization. Allergy. 2001;56:86-7.
198. Leynadier F, MD, Herman D, Vervloet D, Andre C. Specific immunotherapy with a standardized latex extract versus placebo in allergic healthcare workers. J Allergy Clin Immunol. 2000;106:585-90.
199. Tabar AI, Anda M, Bonifaci F, Bilo B, Leynadier F, Fuchs T, Ring J, Galvain J, André J. Specific immunotherapy with standardized latex extract versus placebo in latex allergic patients. J Invest Allergol Clin Immunol. 2006;141:369-76.
200. Sastre J, Fernández-Nieto M, Rico P, Martín S, Barber D, Cuesta J, de las Heras M, Quirce S. Specific immunotherapy with a standardized latex extract in allergic workers: a double-blind, placebo-controlled study. J Allergy Clin Immunol. 2003;111:985-94.
201. Lombardero M, Barber D, Rico P, Wikborg T, Sastre J. Characterization of latex extract for clinical use. In vitro measurements. J Allergy Clin Immunol. 2000;105:261-2.
202. Cisteró A, Sastre J, Enrique E, Fernandez M, Alonso R, Quirce S, Gandarias B, Parmiani S, Rico P. Tolerance and effects on skin reactivity to latex of sublingual rush immunotherapy with a latex extract. J Invest Allergol Clin Immunol. 2004;14:17-25.
203. Antico A, Pagani M, Crema A. Anaphylaxis by latex sublingual immunotherapy. Allergy. 2006;61(10):1236-7.
204. Lauren Charous B, Blanco C, Tarlo S, Hamilton RG, Baur X, Beezhold D, Sussman G, Yunginger JW. Natural rubber latex allergy after 12 years: Recommendations and perspectives. J Allergy Clin Immunol. 2002;109:31-4.
205. Nieto A, Mazon A, Pamies R, Lanuza A, Muñoz A, Estornell F, García-Ibarra F. Efficacy of latex avoidance for primary prevention of latex sensitization in children with spina bifida. J Pediatr. 2002;140:370-2.
206. Cremer R, Hoppe A, Kleine Diepenbruck U, Blaker F. Longitudinal study on latex sensitization in children with spina bifida. Pediatr Allergy Immunol. 1998;9:40-3.
207. Cremer R, Kleine-Diepenbruck U, Hering F, Holschneider AM. Reduction of latex sensitization in spina bifida patients by a primary prophylaxis programme (five years experience). Eur J Pediatr Surg. 2002;12:S19-21.
208. Cremer R, Kleine Diepenbruck U, Hoppe A, Bläker F. Latex allergy in spina bifida patients--prevention by primary prophylaxis. Allergy. 1998;53:709-11.
209. Niggeman B, Buck D, Michael T, Haberl H, Wahn U. Latex allergy in spina bifida: at the turning point? J Allergy Clin Immunol. 2000;106:1201.
210. Cremer R, Hoppe A, Klein-Diepenbruck U, Blaker F. Effects of prophylaxis on latex sensitization in children with spina bifida. Eur J Pediatr Surg. 1998;8:59.
211. Nakamura CT, Ferdman RM, Keens TG, Davidson SL. Latex allergy in children on home mechanical ventilation. Chest. 2000;118:1000-3.
212. Mazon A, Solera E, Alentado N, Oliver F, Pamies R, Caballero L, Nieto A, Dalmau J. Frequent IgE sensitization to latex, cow's milk, and egg in children with short bowel syndrome. Pediatr Allergy Immunol. 2008;19:180-3.
213. Gentili A, Ricci G, Di Lorenzo FP, Pigna A, Masi M, Baroncini S. Latex allergy in children with oesophageal atresia. Paediatr Anaesth. 2003 Oct;13(8):6-75.
214. Dehlink E, Prandstetter C, Eiwegger T, Putschogl B, Urbanek R, Szepfalusi Z. Increased prevalence of latex-sensitization among children with chronic renal failure. Allergy. 2004 Jul;59(7):734-8.
215. Cremer R, Lorbacher M, Hering F, Engelskirchen R. Natural rubber latex sensitisation and allergy in patients with spina bifida, urogenital disorders and oesophageal atresia compared with a normal paediatric population. Eur J Pediatr Surg. 2007;17:194-8.

216. Pareja Torres MC, De la Iglesia Huerta A. La vigilancia de la salud en usuarios de guantes de protección individual. Prevención, Trabajo y Salud. 2003;26;25-40.
217. Charous BL, Blanco C, Tarlo S, Hamilton RG, Baur X, Beezhold D, Sussman G, Yuginger JW. Natural rubber latex allergy after twelve years: recommendations and perspectives. J Allergy Clin Immunol. 2002;109:31-4.
218. Uso racional del guante de látex. Available at: http/: www.seaic.es.
219. Bousquet J, Flahault A, Vandenplas O, Ameille J, Duron JJ, Pecquet C, Chevrie K, Annesi-Maesano I. Natural rubber latex allergy among health care workers: a systematic review of the evidence. J Allergy Clin Immunol. 2006 Aug;118(2):447-54.
220. Saary J, Kanani A, Alghadeer H, Holness DL, Tarlo SM. Changes in rates of natural rubber latex sensitivity among dental school students and staff after changes in latex globes. J Allergy Clin Immunol. 2002;109:131-5.
221. Hunt LW, Kelkar P, Reed CE, Yunginger JW. Management of occupational allergy to natural rubber latex in a medical center: the importance of quantitative latex allergen measurement and objective follow-up. J Allergy Clin Immunol. 2002;110(Suppl):S96-106.
222. Tarlo SM, Easty A, Eubanks K, Parsons CR, Min F, Juvet S, Liss GM. Outcomes of a natural rubber latex control program in an Ontario teaching hospital. J Allergy Clin Immunol. 2001 Oct;108(4):628-33.
223. Schmid K, Christoph Broding H, Niklas D, Drexler H. Latex sensitization in dental students using powder-free gloves low in latex protein: a cross-sectional study. Contact Dermatitis. 2002;47:103-8.
224. Latza U, Haamann F, Baur X. Effectiveness of a nationwide interdisciplinary preventive programme for latex allergy. Int Arch Occup Environ Health. 2005;78:394-402.
225. 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;110:318-23.
226. Turjanmaa K, Kanto M, Kautiainen H, Reunala T, Palosno T. Long-term outcome of 160 adult patients with natural rubber latex allergy. J Allergy Clin Immunol. 2002;110:S70-4.
227. Merget R, van Kampen V, Sucker K, Heinze E, Taeger D, Goldscheid N, Haufs MG, Raulf-Heimsoth M, Kromark K, Nienhaus A, Bruening T. The German experience 10 years after the latex allergy epidemic: need for further preventive measures in healthcare employees with latex allergy. Int Arch Occup Environ Health. 2010 Dec;83(8):895-903.
228. Vandenplas O, Delwiche JP, Delpechin S, Sibille Y, Vande Weyer R, Delaunois L. Latex gloves with a lower protein content reduce bronchial reactions in subjects with occupational asthma caused by latex. Am J Respir Crit Care Med. 1995;151:887-91.
229. Hamilton RG, Brown RH. Impact of personal avoidance practices on health care workers sensitized to natural rubber latex. J Allergy Clin Immunol. 2000;105:839-41.
230. Vandenplas O, Jemart J, Delwiche JP, Evrard G, Larbanois A. Occupational asthma caused by natural rubber latex: outcome according to cessation or reduction of exposure. J Allergy Clin Immunol. 2002;109:125-30.
231. Yuill GM, Saroya D, Yuill SL. A national survey of the provision for patients with latex allergy. Anaesthesia. 2003 Aug;58(8):775-7.
232. Reines HD, Seifert PC. Patient safety: latex allergy. Surg Clin North Am. 2005;85:1329-40.
233. Steelman VM. Latex allergy precautions. A research-based protocol. Nurs Clin North Am. 1995;30:475-93.
234. Rhodes A. Latex allergy awareness and protocol. Br J Perioper Nurs. 2000 Mar;10(3):157-62.
235. Patriarca B, Korniewicz DM. Latex allergy and implications for urology nursing. Urol Nurs. 1999;19:187-91.
236. de la Hoz B, Gómez J, Sánchez-Cano M, Losada E. Protocolo de adecuación del material anestésico-quirúrgico para pacientes alérgicos al látex. Rev Esp Alergol Inmunol Clin. 1999;14:11-8.
237. Reider N, Kretz G, Menardi G, Ulmert H, Fritsch P. Outcome of a latex avoidance program in a high-risk population for latex allergy – a five year follow-up study. Clin Exp Allergy. 2002;32:708-13.
238. Gentili A, Lima M, Ricci G, Pigna A, Fae M, Di Lorenzo E, Masi M, Baroncini S. Secondary prevention of latex allergy in children: analysis of results. Pediatr Med Chir. 2006;28:83-90.
239. Ylitalo L, Alenius H, Turjanmaa K, Palosuo T, Reunala T. Natural rubber latex allergy in children: a follow up study. Clin Exp Allergy. 2000;30:1611-7.
240. Diéguez MC, Antón M, Blanco R, Pulido Z, Muriel A, de la Hoz B. Allergy to latex in childhood: a follow-up study. Allergologia et Immunopathol. 2006;34:17-22.
241. Levy DA, Moudiki P, Leynadier F. Deproteinised latex condoms are well tolerated by latex allergic patients. Sex Transm Inf. 2001;77;202-3.
242. Schwartz HJ. Latex: a potential hidden "food" allergen in fast food restaurants. J Allergy Clin Immunol. 1995 Jan;95(1 Pt 1):139-40.
243. Beezhold AH, Reschke JE, Allen JM, Kostyal DA, Sussmen GL. Latex Protein: a "hidden" food allergen? Allergy Asthma Proc. 2000;21:301-6.
244. Hughes TM. Natural rubber latex allergy to adhesive in chocolate bar wrappers. Contact Dermatitis. 2001 Jan;44(1):46-7.
245. Fiocchi A, Restani P, Ballabio C, Bouygue GR, Serra A, Travaini M, Terracciano L. Severe anaphylaxis induced by latex as a contaminant of plastic balls in play pits. J Allergy Clin Immunol. 2001;108(2):298-300.
246. Cogen FC, Beezhold DH. Hair glue anaphylaxis: a hidden latex allergy. Ann Allergy Asthma Immunol. 2002;88:61-3.
247. Wakelin SH. Contact anaphylaxis from natural rubber latex used as an adhesive for hair extensions. Br J Dermatol. 2002;146:340-1.
248. Diéguez MC, Cerecedo I, Muriel A, Losada A, García E, Lázaro M, de la Hoz B. Adaptation and validation of the Spanish version of the Quality Of Life in Latex Allergy questionnaire (QOLLA). J Investig Allergol Clin Immunol. 2011;21(4):283-9.
249. Weissman DN, Lewis DM. Allergic and latex-specific sensitization: Route, frequency, and amount of exposure that are required to initiate IgE production. J Allergy Clin Immunol. 2002;110:S57-63.
250. Brown RH; Schauble JF, Hamilton RG. Prevalence of latex allergy among anesthesiologists: identification of sensitized but asymptomatic individuals. Anesthesiology. 1998;89:292-9.
251. Douglas R, Morton J, Czarny D, O'Hehir RE. Prevalence of IgE-mediated allergy to latex in hospital nursing staff. Aust N Z J

Med. 1997;27:165-9.
252. Larese Filon F, Bosco A, Fiorito A, Negro C, Barbina P. Latex symptoms and sensitisation in health care workers. Int Arch Occup Environ Health. 2001;74:219-23.
253. Chaiear N, Jindawong B, Boonsawas W, Kanchanarach T, Sakunkoo P. Glove allergy and sensitization to natural rubber latex among nursing staff at Srinagarind Hospital, Khon Kaen, Thailand. J Med Assoc Thai. 2006;89:3-76.
254. Bernardini R, Novembre E, Ingargiola A, Veltroni M, Mugnaini L, Cianferoni A, Lombardi E, Vierucci A. Prevalence and risk factors of latex sensitization in an unselected pediatric population. J Allergy Clin Immunol. 1998;101:621-5.
255. Crippa M, Gelmi M, Sala E, Zefferino R, Baccolo TP, Alessio L. [Latex allergy in health care workers: frequency, exposure quantification, efficacy of criteria used for job fitness assessment]. Occup Environ Med. 2006;63:121-5. Italian.
256. Nguyen B, Ghezzo H, Malo JL, Gautrin D. Time course of onset of sensitization to common and occupational inhalants in apprentices. J Allergy Clin Immunol. 2003;111:807-12.
257. Archambault S, Malo JL, Infante-Rivard C, Ghezzo H, Gautrin D. Incidence of sensitization, symptoms, and probable occupational rhinoconjunctivitis and asthma in apprentices starting exposure to latex. J Allergy Clin Immunol. 2001;107:921-3.
258. Phillips VL, Goodrich MA, Sullivan TJ. Health care worker disability due to latex allergy and asthma: a cost analysis. Am J Public Health. 1999;89:1024-8.
259. Moneret-Vautrin DA, Beaudouin E, Widmer S, Mouton C, Kanny G, Prestat F, Kohler C, Feldmann L. Prospective study of risk factors in natural rubber hypersensitivity. J Allergy Clin Immunol. 1993;92:68-77.
260. Rihs HP, Chen Z, Cremer R, Baur X. HLA class II antigens DR4 and DQ8 are associated with allergy to hevein, a major allergen of Hevea latex. Tissue Antigens. 1997;49:92-5.
261. Rihs HP, Cremer R, Chen Z, Baur X. Molecular analysis of DRB and DQB1 alleles in German spina bifida patients with and without IgE responsiveness to the latex major allergen Hev b 1. Clin Exp Allergy. 1998;28:175-80.
262. Rihs HP, Chen Z, Ruëff F, Cremer R, Raulf-Heimsoth M, Baur X, Moneret-Vautrin DA, Brüning T. HLA-DQ8 and the HLA-DQ8-DR4 haplotype are positively associated with the hevein-specific IgE immune response in health care workers with latex allergy. J Allergy Clin Immunol. 2002;110:507-14.
263. Blanco C, Sánchez-García F, Torres-Galván MJ, Dumpierrez AG, Almeida L, Figueroa J, Ortega N, Castillo R, Gallego MD, Carrillo T. Genetic basis of the latex-fruit syndrome: association with HLA class II alleles in a Spanish population. J Allergy Clin Immunol. 2004;114:1070-6.
264. Brown RH, Hamilton RG, Mintz M, Jedlicka AE, Scott AL, Kleeberger SR. Genetic predisposition to latex allergy: role of interleukin 13 and interleukin 18. Anesthesiology. 2005;102:496-502.
265. Korniewicz DM, Chookaew N, El-Masri M, Mudd K, Bollinger ME. Conversion to low-protein, powder-free surgical gloves: is it worth the cost? AAOHN J. 2005;53:388-93.
266. Beezhold DH, Hickey VL, Sussman GL. Mutational analysis of the IgE epitopes in the latex allergen Hev b 5. J Allergy Clin Immunol. 2001;107:1069-76.
267. Karisola P, Alenius H, Mikkola J, Kalkkinen N, Helin J, Pentikäinen OT, Repo S, Reunala T, Turjanmaa K, Johnson MS, Palosuo T, Kulomaa MS. The major conformational IgE-binding epitopes of hevein (Hev b6.02) are identified by a novel chimera-based allergen epitope mapping strategy. J Biol Chem. 2002 Jun21;277(25):22656-61.
268. Raulf-Heimsoth M, Chen Z, Rihs HP, Kalbacher H, Liebers V, Baur X. Analysis of T-cell reactive regions and HLA-DR4 binding motifs on the latex allergen Hev b 1 (rubber elongation factor). Clin Exp Allergy. 1998 Mar;28(3):339-48.
269. de Silva HD, Sutherland MF, Suphioglu C, McLellan SC, Slater JE, Rolland JM, O'hehir RE. Human T-cell epitopes of the latex allergen Hev b 5 in health care workers. J Allergy Clin Immunol. 2000 May;105(5):1017-24.
270. Bohle B, Wagner B, Vollmann U, Buck D, Niggemann B, Szépfalusi Z, Fischer G, Scheiner O, Breiteneder H, Ebner C. Characterization of T cell responses to Hev b 3, an allergen associated with latex allergy in spina bifida patients. J Immunol. 2000 Apr 15;164(8):4393-8.
271. Hunt LW, Kelkar P, Reed CE, Yunginger JW. Management of occupational allergy to natural rubber latex in medical center: The importance of quantitative latex allergen measurement and objective follow-up. J Allergy Clin Immunol. 2002;110:S:96-106.
272. Kearns CF, Norris A. Latex allergy and plastic syringes. Anesth Analg. 1996;82:429.
273. Kam PC, Lee MS, Thompson JF. Latex allergy: an emerging clinical and occupational health problem. Anaesthesia. 1997;52:570-5.
274. Preventing allergic reactions to natural rubber latex in the workplace. US Department of Health and Human Services, Public Health Service, Centers for Disease Control Prevention, National Institute for Occupational Safety and Health. Cincinnati: Government Printing Office, 1997. DHHS (NIOSH) publication no. 97-135.
275. Thomsen DJ, Burke TG. Lack of latex allergen contamination of solutions withdrawn from vials with natural rubber stoppers. Am J Health Syst Pharm. 2000 Jan 1;57(1):44-7.
276. Jones JM, Sussman GL, Beezhold DH. Latex allergen levels of injectable collagen stored in syringes with rubber plungers. Urology. 1996 Jun;47(6):898-902.
277. Fiocchi A, Restani P, Ballabio C, Bouygue GR, Serra A, Travaini M, Terracciano L. Severe anaphylaxis induced by latex as a contaminant of plastic balls in play pits. J Allergy Clin Immunol. 2001 Aug;108(2):298-300.
278. Pumphrey RS, Duddridge M, Norton J. Fatal latex allergy [Letter]. J Allergy Clin Immunol. 2001;107:558.
279. European Commission. Opinion on natural rubber latex allergy; adopted by the Scientific Committee on Medical Products and Medical Devices on 27 June 2000. http://europa.eu.int/comm/food/fs/sc/scmp/out31_en.pdf.

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