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Natural Rubber Latex Allergy

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1. Introduction

Natural rubber latex (NRL) is a milky fluid from the *Hevea brasiliensis* (Hev b) tree, which functions as a protective sealant (Ownby, 2002). Because of its excellent elastic properties, it is widely used in the manufacture of medical devices and in a variety of everyday articles such as gloves, condoms, balloons, baby nipples, syringe plungers, and vial stoppers. As many as 40 000 types of consumer products may contain NRL (Perkin et al., 2000). The use of rubber for surgical gloves was first made in 1984 by Richard Cook and who popularized the use of rubber gloves in surgery was William Hasted (Dyck, 2000).

NRL allergy is a common occupational disease. The induction of latex allergy commonly occurs after exposure of skin or mucous membrane to natural rubber latex. It is usually a contact dermatitis or delayed allergy (type IV), and reaction mediated by IgE (type I) or immediate hypersensitivity. Latex allergy symptoms can be mild or severe and manifest as contact urticaria, rhinoconjunctivitis, asthma, and mucosal swelling; systemic reactions consist of generalized urticaria and anaphylactic shock (Hamann et al., 1998; Agarwal & Gawkrodger, 2002; Cao et al., 2010; Cleenewerck, 2010).

It affects people who are frequently exposed to products made of natural rubber latex, such as health care workers HCWs (5 to 17%); and groups at high risk included spina bifida cystica patients (to almost 65%), latex industry workers, specific food-allergy patients, and patients with a history of atopy or multiple surgical procedures (Nettis et al., 2002; Turjanmaa et al., 2002; Sullivan, 2005; Sukekava & Sell, 2007; Armentia et al., 2010; Bains et al., 2010; Radauer et al., 2011).

Knowledge about latex allergy is important for three reasons: firstly, it is potentially fatal if the patient is not properly managed; secondly, it is common in healthcare workers (HCWs) as an occupational disease; and thirdly, its incidence has been increasing due to increased use of latex gloves as a barrier against viral infections (Agarwal & Gawkrodger, 2002). Also, latex has cross reactivity to banana, avocado, kiwi and other foods.

Undiagnosed latex allergy is potentially very serious for patients and is increasingly recognized as a significant contributor to morbidity and mortality during medical and surgical procedures, and anaphylactic shock has been documented (Kosti & Lambrianidis, 2002; Sonofuchi et al., 2010).

At present, latex avoidance is the only available treatment and is the key to preventing allergic reactions in latex-sensitized individuals.

This chapter will present the etiology, epidemiology, and pathogenesis of natural rubber latex allergy.

2. Latex allergens

Latex products are ubiquitous in our environment and its use and choice is attributed to its biomechanical performance characteristics, which include strength, elasticity, tear resistance, and superior barriers qualities.

Raw latex is a milky sap harvested from the rubber tree *(Hevea brasiliensis)* and it is subsequently vulcanized into elastic rubber with which we are all familiar. This milky substance is the cytoplasm of the cells of the lactiferous system of the tree. The vast majority of *Hevea brasiliensis* cultivation occurs in Malaysia, Indonesia and Thailand. After harvest by sap collection, NRL is ammoniated to prevent bacterial contamination and coagulation, resulting in the hydrolysis to latex proteins. Prior to use in manufacturing, the latex is formulated by the addition of multiple chemicals: accelerators, antioxidants, and secondary preservatives. Thus human exposure is a mixture of residual chemicals and hydrolyzed latex peptides. The proteins components have been responsible for type I latex-specific allergy and the accelerators and antioxidants are agents of type IV allergic reactions (contact dermatitis). Not until Charles Goodyear developed the process of vulcanization to stabilize rubber and prevent it from easily melting or freezing, did the rubber industry become important (Dyck, 2000).

The essential structural functional unit in processed latex is an aqueous elastomer emulsion containing mainly cis-1,4-polyisoprene (30%-40%) and water (55%-65%), which is coated with a layer of protein, lipid, and phospholipids. The protein content of rubber tree sap is approximately 15mg/ml and includes more than 240 polypeptides, and 60 of these react to latex-specific IgE. Latex proteins can be divided into: water-soluble proteins, starch-bound proteins, and latex-bound proteins. Of the multiple proteins found in latex, certain specific proteins have been identified as being the major concern in causing IgE-mediated allergic reactions. Fourteen proteins have been identified, characterized, and officially accepted as allergenic components (Sussman & Beezold, 1994; Lee et al., 2010; Ott et al., 2010).

The WHO_International Union of Immunological Societies Allergen Nomenclature Committee (www.allergens.org) listed 14 NRL Hev b allergens (Hev b 1-14) characterized at the molecular level. It has included Hev b 1, rubber elongation factor (Chen et al., 1997); Hev b 2, b-1,3-glucanase (Yagami et al., 2002); Hev b 3, small rubber particle protein - a 24-kDa protein (Wagner et al., 1999); Hev b 4, a component of the microhelix protein complex – lecithinase homologue; Hev b 6, prohevein/hevein precursor; Hev b 7; patatin-like protein; and Hev b 13, esterase (Beirnstein et al., 2003); Hev b 5, acidic protein – proline-rich protein (Slater et al., 1996); Hev b 8, profiling (Nieto et al., 2002); Hev b 9, enolase (Wagner et al., 2000); Hev b 10, manganese superoxide dismutase (Rihs et al., 2001); Hev b 12, non-specific lipid transfer protein 1 (Beezhold et al., 2003); and Hev b 11, class I chitinase, and Hev b 14, hevamine, that no allergenicity has been described yet. The epitopes identified as IgE-binding areas have been defined (Pedraza-Escalona et al., 2009; Rougé et al., 2010). Natural rubber latex (NRL) allergenic proteins are listed in Table 1.

It has been suggested that Hev b 1 and Hev b 3 are major allergens in children with spina bifida and urological congenital anomalies (Baur et al., 1995; Yeang et al., 1996; Chen et al., 1997). Berstein et al. (2003) identified Hev b 2, 5, 6.01 and Hev b 13 as the major *in vivo* allergens among HCWs with allergy to NRL, confirmed by percutaneous sensitivity to nonammoniated latex (NAL). These differences of epitopes reactivity can be explained by the different allergen profiles on internal and external surfaces of natural rubber latex gloves (Peixinho et al., 2008).

Biochemical name	Allergen name	WM		Allerginicity reference
Rubber elongation factor	Hev b 1	14	mainly associated with spina bifida patients	Chen et al., 1997
b-1,3-glucanase	Hev b 2	34	linked more to adult latex-allergy patients	Yagami et al., 2002
Small rubber particle protein	Hev b 3	24	mainly associated with spina bifida patients	Wagner et al., 1999
Lecithinase homologue	Hev b 4	53-55		Beirnstein et al., 2003
Acidic protein	Hev b 5	16	linked more to adult latex-allergy patients	Slater et al., 1996
Hevein precursor	Hev b 6	20	linked more to adult latex-allergy patients	Beirnstein et al., 2003
Patatin-like protein	Hev b 7	42		Beirnstein et al., 2003
Profilin	Hev b 8	15		Nieto et al., 2002
Enolase	Hev b 9	51		Wagner et al., 2000
Superoxide dismutase (Mn)	Hev b 10	26		Rihs et al., 2001
Class I chitinase	Hev b 11	30	no allergenicity described	
Non-specific lipid transfer protein 1	Hev b 12	9		Beezhold et al., 2003
Esterase	Hev b 13	42	linked more to adult latex-allergy patients	Beirnstein et al., 2003
Hevamine	Hev b 14	30	no allergenicity described	

Table 1. Natural rubber latex (NRL) allergenic proteins

3. Hypersensitivity reactions

Specific immune responses are normally stimulated when an individual is exposed to a foreign antigen and this process is called immunization. Immune responses are specific for different structural components of the most complex proteins and polysaccharides antigens. The portions of such antigens are specifically recognized by distinct lymphocytes are called epitopes. This fine specificity exists because T and B lymphocytes express membrane receptors that distinguish subtle difference between distinct antigens. *Naïve* lymphocytes are continually released from the primary lymphoid organs into the periphery (secondary lymphoid organs). Antigen-binding can lead to activation of a T or B cell. All of the progeny cells derived from any single *naïve* lymphocytes that constitute a clone.

Responses to most immunogens can begin only after the immunogen has been captured, processed, and presented by an APC (antigen-processing cell) to CD4 T cells (T_H0). The reason of this is that T cells only recognize immunogens that are bound to major histocompatiblity complex (MHC) proteins on the surfaces of other cells. There are two different classes of MHC proteins. Class I MHC proteins are expressed virtually by all somatic cell types and are used to present substances to CD8 T cells, most of which are cytotoxic T cells. Class II MHC proteins, on the other hand, are expressed only by macrophages and a few other cells types and are necessary for antigen presentation to CD4 T cells - the subset that includes most helper cells. Since helper-cell activation is necessary

for virtually all responses, the class II-bearing APCs plays a pivotal role in controlling such responses.

Exogenous immunogens can be captured in a variety of ways. After captured by APCs become enclosed within membrane-lined vesicles in the cytoplasm and, within these vesicles, undergo a series of alterations called antigen processing and a limited number of the resulting peptides associated non-covalently with class II MHC proteins and transported to APC surface, where they can be detected by CD4 T cells. This process is called antigen presentation. At specific antigen recognition the sequences of events induced in lymphocytes initiate the activation phase. First, the lymphocyte proliferate, leading to expansion of the clones of antigen-specific lymphocytes and amplification of the protective response. Second, lymphocytes differentiate to cells that functions are to eliminate foreign antigens: thus, B cells transform to plasma cells that secret specific antibody that binds to soluble antigen; and some T cells (CD4 or T helper) differentiate into cells that activate phagocytes to kill intracellular antigens, and other T cells (CD8) that directly lyses cells that are producing foreign antigens such as viral proteins. The effector phase is the stage that activated performs the functions that lead to elimination of the antigens: inflammatory response is amplified after recruitment of specific and nonspecific effectors cells (lymphocytes, macrophages, basophiles, mast cells) and their soluble components production (lymphokines, monokines, complement, kinines, arachidonic acid derivates, and mast cells- basophile products).

The immune response serves to protect the individual from foreign antigens with a well-controlled immune and inflammatory response. However damage to host tissues and diseases can result from dysfunction of any component of the host defense system, like hypersensitivity or allergy.

The allergy results when an exposure to the allergens induces an immune response, referred to as “sensitization” rather than immunization. Once sensitization occurs, an individual will be not symptomatic until there is a new exposure to the same allergen. Then the reaction of allergen with specific antibody or sensitized effector T lymphocyte induces an inflammatory response, producing the symptoms and signs of the allergic reaction.

The reactions characteristic of type I hypersensitivity are dependent on the specific triggering of IgE-sensitized mast cell by allergen. The sensitization occurs when foreign antigens or allergens enter in the host, are processed and presented to APC to the T helper 2 (T_H2) cells. T_H2 cells secrete cytokines (interleukins: IL-4, IL-5 and IL-6) that induces B cells proliferation and favour to production of an allergens specific-IgE response. IgE binds, via Fc_ε receptors, to mast cells and basophiles thus sensitizing them. When allergen subsequently reaches the sensitized mast cells it cross-links surphace-bound IgE and increases intracellular calcium that triggers the release of pre-formed mediators, such as histamine and proteases, and newly synthesized, lipid-derived mediators such as leukotrienes and prostaglandins. These autacoids produce the clinical symptoms of allergy (asthma, eczema, and anaphylaxis).

Type IV (delayed) hypersensitivity reactions involve cell-mediated immune reactions rather than humoral response. The sensitization occurs when Langerhans cells process foreign antigens and present them to T helper 1 (T_H1) cells. The T cells responsibly for the delayed response have been specifically sensitized by a previous encounter, and act recruiting other cell types to the site of the reaction. Contact hypersensitivity is characterized by an eczematous reaction at the point of the contact with an allergen.

4. Latex sensitization

Sensitization and development of latex allergy arise from exposure to products containing residual latex proteins and chemical additives in latex products. Latex proteins are potent allergens capable of inducing fatal anaphylaxis.

Sensitization of latex allergy can occur through the skin, by inhalation or by internal exposure (mucous membranes of the mouth, vagina or rectum). Medical devices (anesthetic masks, condom catheters, ileostomy bags, balloon catheters used for enemas and latex gloves) can induce sensitization and then subsequently cause an allergy to develop on re-exposure. The addiction of cornstarch powder of gloves, in 1947, to prevent sticking and give a smoother fit, has been shown to increase the leaching of latex proteins and exposure latex proteins on the surface. Powder from latex gloves serves as vector of the dangerous proteins that then trigger an allergic response. Cornstarch also promotes aerosolization of the latex proteins when gloves are removed, and its release powder into the air and latex proteins are inhaled by all individuals in the room. Rubber is extensively distributed in the environment and we are in contact with it virtually all the time.

Latex absorption through the skin is postulated as the major route of sensitization in health care workers by the soluble proteins. Friction, pressure, heat, and perspiration are among the nonspecific factors that influence the occurrence, severity, and sites of involvement of hypersensitivity and cutaneous manifestations.

5. Pathogenesis and clinical manifestations

Clinical manifestations include irritant contact dermatitis, allergic contact dermatitis (type IV), and immediate hypersensitivity reaction mediated by IgE (type I) (Table 2). It can affect the skin, eyes and lungs (Nutter, 1979; Hamann et al., 1998; Mebra & Hunter, 1998; Agarwal & Gawkrodger, 2002; Cao et al., 2010; Cleenewerck, 2010).

5.1 Irritant contact dermatitis

Irritant contact dermatitis (ICD) is not an allergic reaction. It occurs when an exogenous substance without previous sensitization causes direct damage to the skin. Usually it is the result of contact with glove additives. Chapped skin from hand washing can be responsible for this symptom. Early manifestations of this type of reaction include itchy (most common symptoms), but morphological features (dry, crusted lesions) are similar in allergic dermatitis, especially on fingers webs and under rings. Greater degrees of irritation result in burning, red or swollen tissues. Vesiculation is a late manifestation, but rarely occurs. ICD has a diagnosis for exclusion, and patch testing is negative. Management includes careful hand washing techniques, use of skin emollients, and an effective routine.

5.2 Type IV hypersensitivity - Delayed reactions

Delayed (type IV) allergy or contact dermatitis to rubber gloves is primarily caused by accelerators added to speed up rubber vulcanization, including carbamates, thiurams, 2-mercaptobenzothiszole, and 1,3-diphenylguanidina. It may also cause by antioxidants that prevent rubber deterioration, such as black rubber mix chemicals (*p*-phenylenediamines (Cao et al., 2010). It typically manifests within 24 to 48 hours after contact with the allergen. It is localized to the skin or mucous membrane. The patient presents a diffuse or patchy eczema on the dorsal surface of the hands, wrists, and distal forearms. Latter the reaction

can become generalized, and chronic exposure leads to hyperkeratosis and lichenification, and at times either hyper- or hypopigmentation. The scalp and palms have a greater resistance to contact allergic and irritant reactions than other skin areas. The eyelids, penis, and scrotum often show erythema and edema rather than vesiculation. Patch testing is positive in these patients. The development of a type IV hypersensitivity allergic response may occur after years of contact with the substance.

5.3 Type I hypersensitivity - Immediate reactions

Type I reactions to latex involve specific immunoglobulin IgE and mediators of anaphylaxis. It is caused by latex proteins that direct sensitize the patients, and reactions occur within 1-30 minutes. There may be a wide spectrum of clinical presentations. The route of latex antigen presentation will usually dictate the clinical manifestations. The skin manifestations include itching, swelling, localized pruritus and urticaria (direct contact). Respiratory involvement consists of sneezing, wheezing and rhinitis; and the eyes may water, itch and conjunctivitis (aerosol exposure or facial contact – latex proteins are adsorbed on gloves powder that becomes airborne and can be directly inhaled). A mucosal route of exposure to latex allergens is often associated with anaphylactic reactions. The clinical manifestations may be serious and give rise to a generalized shock-like reaction: systemic reactions such as broncospasm, hypotension, cardiorespiratory collapse, and shock can occur with more substantial exposure and in extremely sensitive individuals.

Contact urticaria is the most common early manifestation of rubber allergy, particularly in latex-sensitive health care workers. Symptoms appear within 10-15 min after donning gloves. No residual coloration occurs after resolution of the urticaria.

Anaphylactic shock is potentially fatal and anaphylactic response to latex exposure occurs most commonly intraoperatively. However, anaphylactic reactions have been encountered during gloving, exposure to dental dams, condom use, and even after indirect exposition by contact with individual who use latex gloves. The response appears minutes after the administration the allergen, manifesting as a respiratory distress, followed by vascular collapse and shock. Cutaneous symptoms, pruritus and urticaria, often occur with or without angioedema. Gastrointestinal manifestations involved nausea, vomiting, crampy abdominal pain, and diarrhea.

Non-Immunological and Immunological Reactions	**Symptoms**	**Etiology**	**Allergens**
Irritant Contact Dermatitis	Irritant contact dermatitis	Non-immunological	Gloves additives
Type I hypersensitivity Immediate reactions	Contact urticaria, asthma, rhinithis, angioedema, generalized anaphylaxis	IgE antibody produced by B cells	Latex proteins
Type IV hypersensitivity Delayed reactions	Contact dermatitis	T cells sensitized to antigens	Chemicals used in manufacture of latex

Table 2. Pathogenesis and clinical manifestations to the allergy of latex

6. Incidence of latex allergy

Latex allergy is now an important medical, occupational, medico-legal and financial problem, and it is essential that policies are developed to reduce it.
The diffusion of the "universal precautions", promoted in 1987 by the Center for Disease Control and Prevention, dramatically increased the use of latex glove in health care workers (HCWs) to reduce the risk of infection, for protection against the HIV and HBV. The increased demand caused an increased production of gloves, and a different chemical treatment of rubber trees which lowered the glove quality, that means high levels of antigens and high powder content. This situation causes an increase of allergic frequency (type I and type IV) and irritant reactions to latex gloves in health care workers.
The prevalence of latex allergy in the general population was estimated at 0.7%-1% in the most reports, but some reports now show numbers up to 6%. A high prevalence of latex hypersensitivity is observed in certain occupational and other high-risk groups with frequent exposure to NRL products, including health care workers (ranges from 2.8% to 17%), operating room personal (15-20%), rubber industry workers (near 10%), spina bifida cystica patients (to almost 65%), atopic individuals (7%), and those who have had multiple surgical operations (6.5%), patients with congenital urologic abnormalities, and those with a coexisting food allergy, most often related to certain fruits. The risk is associated with the peoples who are frequently exposed to products made of natural rubber latex such as in different regions, age, sex and ethnic groups.

6.1 General population

Although data is difficult to obtain, estimates now indicate that 1% to 6% of the general population has some sensitivity or allergy to latex. In 1994, Ownby et al. measured latex-specific IgE in the serum from 1000 blood donors and 6.5% were positive. Prevalence of positive samples was not associated to race or age.

6.2 Risk groups

6.2.1 Health care workers

The major source of workplace exposure has been powered natural rubber latex gloves used mainly by HCW. It has been a problem especially for HCW working in surgical areas or in places where there is more use of latex gloves, in function of the high levels of airbone latex particles in these areas. The prevalence of immediate latex allergy increased with increasing duration of latex exposure. Studies have reported a prevalence of latex sensitization of from 2.8 to 17% of the hospital workpopulation.
The first scientific work describing dermatitis from rubber gloves was published in 1933 (Downing, 1933). Nutter (1979) was the first investigator to describe contact urticaria to rubber gloves: the condition occurred in a house-wife with atopic dermatitis, and during the exacerbation of her hand eczema she noted intensive itching for her hands which occurred 5 min after donning a pair of rubber gloves. The urticaria was confirmed by a patch test using a small piece of rubber gloves and with a skin prick test. One year later, Förström described the first case of contact urticaria from latex surgical gloves in a nurse with history of atopic dermatitis and allergic rhinitis.
In 1987, Turjanmaa was the first to evaluate the frequency of latex gloves allergy among health care workers. A total of 512 hospital employees were screened by using a latex gloves scratch-chamber test and subsequent prick test for individuals who are positive in

screening. Twenty-three (4.5%) had positive scratch-chamber test, and the prick test was positive in 15 of these 23 patients. Most of them had a personal history of atopy, asthma, allergic rhinitis, and atopic eczema. Latex gloves allergy was significantly more frequent in personal of operative room.

Arellano et al. (1992) were the first to report the prevalence of latex sensitization among physicians using latex gloves in a North American Hospital setting. Using a latex skin prick test they determined the sensitization in 9.9% of the North American physicians.

Since 1987, the number of HCW with positive test results for NRL has been increased. In 1994, Charous et al. reviewed medical histories of symptomatic workers with occupational exposure to latex and they evidenced that the number of patients reporting onset of latex-induced contact dermatitis had remained relatively constant, whereas the number of the patients with contact dermatitis and systemic reactions had markedly increased.

Some reports about prevalence of latex allergy in HCW in different countries are presented. At an Italy Hospital, a high prevalence of rubber glove-induced dermatoses among the employees were evidenced: about of 24% the health care workers, who used or had used latex gloves at work, reported glove-induced symptoms, namely, cutaneous symptoms in all the cases. Non-cutaneous symptoms appeared in 8.1%. Positive patch tests to rubber-related allergens were exhibited at 10.5% of symptomatic employees (Nettis et al., 2002).

The prevalence of latex allergy among HCWs in Russia, and adjacent eastern European countries was available and considerably less than reported in Western Europe and the United States. Skin test to latex was positive in 5.4% of HCWs and 1.9% were classified as latex-allergic based on positive skin tests to latex associated with allergy symptoms with exposure. Some of them had experienced anaphylactic reactions to latex. The low prevalence of latex allergy suggests that lessened exposure to natural latex powdered gloves in HCWs in Russia (Nolte et al., 2002).

To assess the allergic risk induced by latex gloves in HCWs, a meta-analysis was carried out under the auspices of the French National Regulatory Authority. Latex allergy was found in 4.32% (range, 4.01% to 4.63%) of HCWs and in 1.37% (range, 0.43% to 2.31%) of the general population. Latex-positive skin prick test responses ranged from 2.1% to 3.7% in the general population and from 6.9% to 7.8% for the HCWs (Bousquet et al, 2006).

To determine the main factors associated with latex allergy and to quantify levels of airborne latex particles in different areas of Spanish hospital, a cross-sectional study was conducted by Diéguez et al. (2007). More allergic patients were found in the surgery department, intensive care unit, and vascular radiology unit.

In Taiwan, natural rubber latex is the most important occupational allergen among medical workers. To evaluate immediate latex allergy and contact dermatitis, 1253 medical workers were interviewed using a screening questionnaire and skin prick testing with commercial latex extract was performed. The prevalence of contact hand dermatitis from latex gloves was 35%. Twelve percent had positive latex skin prick test, suggesting that they had been sensitized to latex proteins. Seventy nine subjects (6%) had immediate allergic reactions to latex products (Lin et al., 2008).

The prevalence of hypersensitivity to natural rubber latex and potential food cross reactions in operation room personnel in Shiraz hospitals revealed a significant correlation between those with positive skin tests to latex with atopia, urticaria, and food hypersensitivity. About 18% of operating room personnel showed positive latex skin tests. The prevalence did not vary by sex, age, education, surgical and non-surgical gloves users, or history of contact dermatitis (Nabavizadeh et al., 2009).

Dates from Asia countries with regard to latex allergy are scarce. Amarasekera et al. (2010) determined the prevalence and risk factors among healthcare workers in a hospital in Sri Lanka. Symptoms suggestive of latex allergy were reported in 16% of the subjects. A considerable proportion (11.4%) of workers had been suffering from latex allergy for more than 5 years.

Oral health care professionals have been shown to be at risk for developing a type I allergy to natural rubber latex (NRL). The prevalence of this allergy in dental hygienists has been evaluated. Hamann et al. (2005) investigated by screened positive for a type I allergy to NRL (SPT-positive) 582 participants to 2000-2002 American Dental Hygienists' Association (ADHA) national meetings. Risk factors and symptom assessments were questioned and were based on a self-reported health history. About 5% screened positive for a type I allergy to NRL (SPT-positive). They observed that the NRL allergy was significantly more likely to report an allergy to cross-reacting foods, plants, moulds, and pollens, and to report reactions to rubber products. Sukekava & Sell (2007) determined the incidence of latex gloves allergy among dental care workers. Latex gloves reaction occurred in 19% of them, and 5% reported allergic reactions to other latex products; 2.5% reported symptoms suggesting contact dermatitis and anaphylaxis hypersensitivities, 1.5% reported contact dermatitis, and 1% reported anaphylaxis symptoms when wearing them.

6.2.2 Latex industry workers

Latex industry workers have an increased prevalence of chronic respiratory symptoms and reduced lung function. In 1988, Bascom et al. described a spectrum of respiratory illness associated with eosinophilia that occurred in a group of rubber workers exposed to fumes from a synthetic rubber-based curing operation. Two years latter, 81 latex industry workers were evaluated, and 7 had spirometric changes consistent with asthma, and two of them had positive skin prick test to latex. To known the relation of rubber tree dust exposure to respiratory and skin symptoms, asthma and lung function in regard to wood dust from the rubber tree, a cross-sectional study was carried out among 103 workers in a rubber tree furniture factory and 76 office workers in four factories in Thailand. Factory workers showed increased risk of wheezing, nasal symptoms and asthma compared to office workers. There was a dose-dependent increase in wheeze and skin symptoms in regard to dust level. Significantly increased risks of nasal symptoms and asthma were detected in the low exposure category (Sripaiboonkij et al., 2009).

6.2.3 Patients with spina bifida cystica

Patients with spina bifida cystica form a population at highest risk of latex allergy. Management of infants with spina bifida cystica involves different procedures that include immediate operative skin closure of an open or thin walled defect, ventriculoperitoneal shunting of hydrocephalus, bracing of the lower extremities, and other surgical procedures to address sensory deficits, bowel and bladder dysfunction, pain elimination, orthopedic problems, and minimize or prevent associated neurologic defects. The major risk factors for latex sensitization in spina bifida cystica children include atopy, familiarity propensity for allergy, and very early exposure with mucosal absorption of allergen related to number of surgical procedures. Kelly et al. (1991) pointed out in their studies that spina bifida pediatric patients have 500 times greater a risk of latex-related anaphylaxis during operative

procedures than of the general pediatric population: eight of the 10 pediatric patients experiencing anaphylaxis during surgery. Prevalence of latex sensitivity among the spina bifida cystica pediatric population was among 40 to 65%. The recommendation is that children with spina bifida avoid contact with NRL products from birth.

7. Cases reports of latex-induced anaphylactic reactions

The prevalence of latex allergy is increasing in general population and surgical patient individuals. Several anaphylactic events during some surgical procedures are still rare; however they are associated with increased morbidity and mortality. Undiagnosed latex allergy is potentially very serious for patients. The risk factors for latex skin sensitization were: a previous history of atopy and asthma; history of surgery; pre-existing hand dermatitis; work-related symptoms; and positive skin tests to common inhalant and certain foods. Avoidance of exposure to the allergen is essential to minimizing preoperative complications in patients suspect to be at risk.

In 2003, Verdolin et al. described an accidental diagnosis of latex allergy after urological surgery under spinal anesthesia when patient presented clinical manifestation of anaphylactic shock: confusion, dyspnea, generalized pruritus and erythema, bronchospasm, arterial hypotension, and tachycardia. In Japan, Ueda et al. (2008) reported an anaphylactic reaction to latex forty-three minutes subsequent to spinal anesthesia in a 46-year-old man with a history of atopic dermatitis and bronchial asthma underwent surgery for an inguinal hernia. Sonofuchi et al. (2010) reported anaphylactic shock after introduction of the general anesthesia in the patient who had latex allergy. Machado et al. (2011) described a case of severe latex induced anaphylactic reaction in a patient with a diagnostic suspicion of appendicitis who underwent an emergency surgery under spinal anesthesia. The symptoms occurred approximately 30 minutes after beginning the surgery.

One of the groups that are at risk for anaphylactic reactions to latex during surgical and medical procedures is represented by the obstetric and gynecologic population. A case was reported when an anaphylactic reaction to latex occurred in a pregnant woman patient who underwent a caesarean section that the diagnosis of latex allergy was missed. Following day the woman underwent a surgical re-exploration complicated by fatal cardiovascular arrest. At post-mortem examination, pulmonary mast cells in the bronchial walls and capillary septa were identified, and a great number of degranulating mast cells with tryptase-positive material outside the cells was documented and the latex-specific IgE test showed a high title. Latex-induced fatal anaphylactic shock was recorded as the cause of death. This case highlights some of the practical difficulties in the initial diagnosis and subsequent investigation of fatal anaphylactic reaction during anesthesia. Anaphylaxis is often misdiagnosed because many other pathologic conditions may present identical clinical manifestations, so anaphylactic shock must be differentiated from other causes of circulatory collapse. Although latex allergy usually has a delayed onset after the start of the surgery and most often a slow onset too, it should be always suspected if circulatory collapse and respiratory failure occur during surgery, even if the patient does not belong to a risk group; in the presence of identified risk factors for latex allergy a well-founded suspicion must be stronger, leading to an immediate discontinuation of the potential trigger (Turillazzi et al., 2008).

8. Immunological cross-reactivity between latex and other products

8.1 Food cross-reactivity

Latex allergy has been reported to be associated with allergy to certain foods. Approximately 30-50% of individuals who are allergic to natural rubber latex (NRL) show an associated hypersensitivity to some plant-derived foods, especially freshly consumed fruits. This association of latex allergy and allergy to plant-derived foods is called latex-fruit syndrome. An increasing number of plant sources have been associated with this syndrome. The most frequently involved are banana, avocado, kiwi, and chestnut, although several others may also be included as peach, grape, pineapple, nuts, figs, passion fruit, celery, citrus fruits, chestnut, peach, tomato, potato and bell pepper. Some studies have found out immunological and clinical cross-reactivity.

The hypothesis is that allergen cross-reactivity is due to IgE antibodies that recognize structurally similar epitopes on different proteins that are phylogenetically closely related or represent evolutionarily conserved structures. Several types of proteins have been identified to be involved in the latex-fruit syndrome. Two of these are higher plant defense proteins. Class I chitinases containing an N-terminal hevein-like domain cross-react with hevein (Hev b 6.02). A beta-1,3-glucanase was identified as an important latex allergen which shows cross-reactivity with proteins of bell pepper and banana. Nine distinct IgE-binding epitopes were identified along the entire amino acid sequence of the major latex allergen Hev b 2 (beta-1,3-glucanase), and a smaller number of IgE-binding epitopic areas was identified on the banana beta-1,3- glucanase, which exhibits a very similar overall conformation and charge distribution. Plant defense-related proteins are relatively conserved in the course of evolution and can supply cross-reactive epitopes. It is important to note that various stresses can stimulate the expression of these proteins, which implies that allergens increase in plants under stressful conditions like severe growing situations and exposure to some kinds of chemicals. Another important NRL allergen, Hev b 7, is a patatin-like protein that shows cross-reactivity with its analogous protein in potato (Wagner and Breiteneder, 2002; Barre et al., 2009).

Axelsson e cols. were one of the first researches to described an association between latex allergy and fruit. They describe a 12-year-old girl who developed rhinoconjuntivitis and itching in the throat after eating stone fruits. Subsequently, she developed angioedema after inflating a rubber balloon (Woods et al., 1997). Recently, anaphylactic shock was related in a woman underwent a cardiac catheter examination, and a Swan-Ganz catheter was inserted. She declared no past history of latex allergy, but did have a banana allergy. Skin prick test showed a positive reaction to an extract of latex gloves an extract of the balloon of a Swan-Ganz catheter (Sekiya et al., 2011). It is necessary to pay attention to not only latex allergy but also fruit allergies with cross-reactivity to latex.

Up to 2 out of 3 spina bifida patients with natural rubber latex (NRL) antibodies have crossreacting IgE-antibody against tropical fruit, due to structural homologies between several NRL antigens and allergenic fruit proteins. To investigate whether the patients were first sensitized against NRL or fruit, Cremer et al. (2011) investigated sera of 96 patients for specific IgE antibody against NRL, banana and kiwi as examples for cross reacting fruit. Only two patients developed antibody against fruit without being sensitized against NRL. In most cases the sensitization against fruit follows the NRL sensitization. There is no need to recommend spina bifida patients without NRL sensitization to primarily avoid tropical fruit.

Allergen cross-reactivity between tobacco and other species of Solanaceae family (tomato, potato, aubergine, and egg plant) have been reported. Armentia et al. (2010) have recently studied IgE response to tobacco in asthmatic patients sensitized to Lolium perenne (Perennial rye grass pollen), and have found that 30% of the tobacco responsive patients also have latex sensitization. They concluded that exist cross-reactivity between latex and tobacco allergens, and smoker patients with IgE response to tobacco may be a risk population for latex sensitization.

8.2 Gutta-percha and gutta-balata

In general dental practice, there is over than 30 products containing latex rubber. The practitioner should be cautions when threatening patients with a history or allergy to latex products. Gutta-percha and gutta-balata, used in endodontic treatment, are derived from the *Paliquium gutta* and *Mimusops globsa* trees, respectively, that are in the same botanical family of the rubber tree *Hevea brasiliensis*. For this reason immunological cross-reactivity between gutta-percha, gutta-balata and NRL were investigated (Costa et al., 2001): no detectable cross-reactivity was observed with any of the raw or clinically used gutta-percha products. In contrast, gutta-balata released proteins that were cross-reactive with latex. Because gutta-balata is sometimes added to commercial gutta percha products, caution should be taken if these products are used in endodontic care of latex-allergic individuals.

Many cases of anaphylaxis reactions occurrence in patient sensitive to latex during endodontic treatment has been reported. Boxer et al. (1994) described a latex-allergic dental hygienist who experienced immediate lip and gingival swelling and diffuse urticaria after the insertion of gutta-percha points into her maxillary molar by a general dentist. Immediately after removal of the gutta-percha, relief of the oral discomfort was noted, and the urticaria resolved several hours thereafter.

9. Genetic predisposition

The intensity of latex exposure, the route of sensitization, the genetically determined susceptibility, or the combination of all may have significant influence on pathogenesis of type I reaction to latex allergens. Although exposure to NRL products is necessary for sensitization, it is not sufficient.

The field of genome-based medicine, which attempts to identify genetic ffactors some individuals have, which may protect them or created problems when they undergo medical intervention, is rapidly evolving and affecting all fields of medical practice. Allergic diseases are dependent on the specific triggering of IgE-sensitized mast cell and their activation resulting in an inflammatory response. Immunological specific mechanism is genetically controlled and some individuals are more susceptible to allergic manifestations. Any steps of immunological and inflammatory reactions could be involved and are target of investigations. Polymorphism in over 30 genes localized on 15 different chromosomes has been associated with human allergy. Although the importance of these genetic components in the development of allergic diseases, susceptibility genes have been difficult to identify given the multigenic nature of this effect. The genetic/ immunologic risk factors of diseases susceptibility, that had been most studied, are the classic and non-classic alleles of the Major Histocompatibility Complex (MHC), and promoter genes of cytokine polymorphisms.

The Major Histocompatibility Complex (MHC), located on chromosome 6p21, is the most polymorphic genetic system in mammalians, and has been studied with regard to a wide variety of diseases of distinct etiology. The fundamental role of the different molecules within the MHC is antigen processing and presentation to the T-cell receptor (TCR), which is crucial for the cell interactions in immune response. In humans, while the classic class I *loci*, HLA-A, -B, and -C, bind peptides of intra-cellular origin and present them to CD8 T cells, the classic class II *loci*, HLA-DR, -DQ, and -DP, primarily bind peptides of extra-cellular origin and present them to CD4 T cells, resulting in cytokine production that drives an antibody production.

Focusing specifically on NRL allergy, Rihs et al. (2002) demonstrated the association between the specific IgE response to the major latex allergen hevein (Hev b 6.02) in HCW with latex allergy and latex-sensitized patients with spina bifida, and HLA class II alleles of DQB1 and DRB1, DRB3, DRB4, and DRB5. The class II HLA-DQB1*03:02 (DQ8) allele and HLA-DQB1*03:02 (DQ8)-DRB1*04(DR4) haplotype were significantly involved in the hevein-specific IgE immune response in HCW with latex allergy. NRL-sensitized patients with spina bifida showed an increase HLA-DQB1*03:02 frequency, but this result was not significant.

Two genes that have been of interest with regard to NRL allergy are *IL13* and *IL18*. IL-13, along with IL-4, is critical for the promotion of allergic response. IL-13 plays an important role in mediating airway hyperresponsiveness in asthma. Binding of IL-4 and IL-13 to the α chain of the IL-4 receptor activates germline transcription of the ε heavy-chain gene locus and isotype switching of B cells to IgE production. IL-18 can stimulate interferon production or enhance cytokines and IgE production. SNPs in these genes have been postulated to influence physiologic functions that are important in development of atopy (Monitto et al., 2010). Genetic predisposition to natural rubber latex allergy in the health care workers was available, and has been shown to be associated with promoter polymorphisms in *IL13* and *IL18* genes when compared with nonatopic controls (Brown et al., 2005). This association was not seen when these patients were genotyped for SNPs in other immunomodulatory genes, including *IL4*, tumor necrosis factor- α and -β, CC chemokine receptor 2 and 5, and toll-like receptor 4. In patients born with spina bifda and or genitourinary abnormalities the association of promoter polymorphisms in *IL13* and *IL18* genes was not observed (Monitto et al., 2010).

10. Diagnosis of latex allergy

To manage latex allergy appropriately, prompt and correct diagnosis is essential, and both *in vivo* and *in vitro* assays have been included. There are two elements to consider in latex allergy diagnosis: history and qualitative and quantitative tests.

10.1 History

The diagnosis of latex requires a thorough and accurate medical history. Screening patients is the first step for minimizing the risk of a latex allergic reaction. It is necessary to have a high index of suspicion, especially for patients in high risk occupations or with medical histories that induce repeated exposure to latex. Patients at special risk are those individuals with frequent or prolonged exposure to latex products. The following points must be considered: history of atopy (general allergies); food allergies (especially bananas, kiwi,

avocados, chesnut, fig, tomato); history of allergic reactions to latex (including hives, swelling, eye/nose symptoms, asthma, and anaphylaxis); and undiagnosed reactions or complications during anesthesia, surgery, or dental work.

The medical clinical history about manifestations is often similar among individuals affected by latex allergy. Onset is often insidious with dermatitis of the hands, which patients attribute to frequent hand washing and irritation. After a short period of time (less than a year) erythema, papulovesiculation, induration, and pruritis emerge within 1-3 hours after onset of gloves use. Among HCW, one may often elicit a history of respiratory symptoms, which is pronounced while at work. For patients presenting contact dermatitis or urticaria, the physician should ask about localization and time of onset of the eruption, morphology, nature of progression, and recurrence or periodicity (Woods et al., 1997).

10.2 Diagnostic testing

Latex allergy can be diagnosed by skin prick testing, latex-specific serum immunoglobulin E testing, glove provocation testing, and patch testing. Both *in vivo* and *in vitro* testing methods have been used to diagnose latex allergy with varying degrees of success.

10.2.1 Skin prick testing (SPT)

The cutaneous test or skin prick tests with latex extracts are commonly used in the diagnostic approach to natural rubber latex allergy. For this, a minute quantity of the allergen is introduced into the dermis to cause a reaction with IgE antibodies fixed to cutaneous mast cells for release of mediators, producing a visible wheal and erythema. After 20 minutes the reactions are graded and recorded. The skin of the back or upper arms can be used. It should be done by trained allergists in a hospital setting with adequate resuscitation and medical support services. Reports of anaphylaxis during SPT for latex allergy emphasize the need to safe testing methods for diagnosis. This test has the advantage of being sensitive, rapid, and cost-effective. Reactivity in SPT is related to the potency of the SPT solution used: as a rule solutions with higher protein and antigen contents gave better results. Commercial extracts are used with good specificity and sensivity. Ammoniated and non-ammoniated latex extracts and Hev b 1, 2, 3, 4, 6.01, 7.01, and 13 allergens and recombinant Hev b 5 (rHev b 5) allergens are commonly used for this purpose. Serial dilutions extracts and NRL allergens were employed in skin testing. It is important to consider that sensitivity and specificity of different commercially available skin prick tests could vary (Bernardini et al., 2008b; van Kampen et al., 2010).

10.2.2 *In vitro* assays for latex-specific IgE

Quantitative measurement of allergen-specific IgE antibodies in serum requires special methods to detect the extremely minute quantities (pictograms per milliliter) found in allergic patients. Sensitive and specific commercial *in vitro* serological assays that have been developed for the diagnosis of IgE-mediated latex allergy include a radioallergosorbent assay – RAST, and enzyme-immunoassay method - ELISA. These occur in a 2-phase (solid/liquid) system using an insolubilized allergen that is incubated first in the test serum to react with latex specific IgE and then in radio, fluoro or enzyme- labeled heterologous anti-human IgE isotype. These tests require purified preparations of allergens (Hev b 1, Hev b 3, Hev b 5 - rHev b 5, Hev b 6.02, Hev b 8, and Hev b 13) and anti-human IgE. The differences in preparations of latex allergen and the existence of possible cross-reacting

antibodies contribute to variance in accuracy of these tests. In atopic individuals, especially in patients with allergies to fruits or vegetables, these serological tests can produce false-positive results. The diagnostic sensitivity and specificity of the latex-specific IgE serology can be less when compared with skin tests (Smith et al., 2007).

10.2.3 Microarray technology

Microarray technology has recently been introduced being a reliable tool for diagnosing latex allergy (Ebo et al., 2010; Ott et al., 2010). A positive specific IgE (sIgE) result for latex does not always mirror the clinical situation and is frequently found in individuals without overt latex allergy. The diagnosis of latex allergy could be established by the combination of recombinant latex components present on the microarray (Hev b 1, Hev b 3, Hev b 5 and Hev b 6.02). The reaction can be performed with different platforms, the ImmunoCAP ISAC microarray and traditional singleplexed ImmunoCAP. Microarray can improve the diagnosis of IgE-mediated latex allergy by discriminating between genuine allergy and sensitization.

10.2.4 Provocation test

Occasionally, it is desirable to test the target (cutaneous, respiratory, or gastrointestinal) tissue responsiveness to the allergen under controlled conditions. Cutaneous provocation tests have been used in patients with suspect latex allergy: they wore a latex glove on one hand and a vinyl glove on the other hand for 15 minutes. Sensitivity is 90%, but some studies have indicated it may be more dangerous than skin testing in very allergic individuals. In the nasal provocation test, changes in nasal airways resistance and visible signs of congestion and rhinorrhea are observed after exposure to quantitative allergen challenge. To examine the responses in patients with positive SPT to nasal provocation test, Unsel et al. (2009) found that nasal provocation test has a sensitivity of 96%, specificity of 100%, negative predictive value of 98% and positive predictive value of 100%.

10.2.5 Path testing

Path testing is helpful in differentiating irritant contact dermatitis from allergic contact dermatitis mediated by type IV hypersensitivity reactions. It's a definitive test for diagnosis of patients with type IV hypersensitivity to latex products using a standard battery of rubber additives. The series of rubber allergen were applied on normal skin, usually on the patient's back or arms, under a small semi occlusive dressing. It is left in place for 24-48 hours. The results are first read in 30 minutes after removing patches, and again 24 or 48 h. The positive reaction can be accepted as the cause of the present eruption. Accelerators evoke positive patch tests in 82% patients with occupationally induced contact dermatitis associated with glove use. The allergens that most commonly yielded positive reactions have been carbamates, 4,4-dithiodimorpholine, thiurams mix, 2-mercaptobenzothiazole, and 1,3-diphenylguanidine (Woods et al., 1997; Bendewald et al., 2010; Cao et al., 2010).

11. Management and treatment

At present, latex avoidance is the only available treatment and has been the key to preventing allergic reactions in latex-sensitized individuals. For patients, avoidance of exposure to the allergen is essential to minimizing perioperative complications (Heitz &

Bader, 2010). In 1998, the Food and Drug Administration (FDA) started to require the labeling of medical devices made from rubber latex; since that time substantial progress had been made in identifying latex-free alternatives.

Avoidance of exposure to allergen is essential to minimizing complications in patients suspected to be at risk. The patient must be aware of the long list of medical and consumer products containing latex. Because there is cross reactivity between latex and fruit antigens, patients should be careful when first consuming these fruits after diagnosis. Procedures performed on latex-sensitive patients should be performed in latex-safe environment. A latex-safe environment is one in which no latex gloves are used; in addition, there must be no latex accessories (masks, rebreathing, cannulas, catheters, adhesives, tourniquets, anesthesia equipment) that come in direct contact with the patients. Prophylactic premedication is used by many centers for surgical patients with high risk of latex allergy. The use must be begin 24 h before surgery. In cases of minor reactions, such as contact dermatitis, the gloves should be removed immediately. For severe cases involving pruritus and erythema, therapy with H_1 antagonists should be initiated; H_2 blockers also can be used. In cases of severe systemic anaphylaxis, initial attention should focus on pulmonary and cardiovascular manifestations of the reaction, because these are the major causes of death.

The health care workers with latex allergy must be protected from adverse reaction to latex. Sensitization to latex antigens is commonly encountered in HCW wearing latex gloves with high latex allergen concentrations and in workers wearing powdered latex surgical gloves. HCW who have contact dermatitis to latex products can avoid it by changing to a different brand of gloves like vinyl and other synthetic gloves. Workers with a documented type I latex allergy must be protected from serious systemic reactions. Basically this involves latex avoidance. Low-protein, in powder-free gloves, decreases the sensitization potential of the latex and avoids some of the granuloma associated with the powder. Latex proteins are adsorbed by glove powder and may be airbone and the use of powder-free gloves can sometimes reduce the aerosol levels. In a review of claims data from 1997 to 2005 about the switch to powder-free latex gloves, Malerich et al. (2008) concluded that it was associated with a significant decrease in workers' compensation for latex-related illness. The cost of gloves increased but was partially offset by a decrease in workers' compensation payments and operating room expenses.

Future strategies must focus not only on the reduction of allergens during latex manufacture and development of suitable non-latex gloves, but also the immunotherapy including desensitization of latex allergic individuals and development of candidate vaccine (Belleri & Crippa, 2008; Bernardini et al., 2008a; Rolland & O'Hehir, 2008; Nettis et al., 2010).

In allergy desensitization treatment, the immune response itself can be altered. In practice, true desensitization is rare: specific IgE- mediated allergy is significantly lessened but not eliminated, even after many years of treatment. Immunological changes during desensitization therapy for IgE- mediated disease consist of increased IgG antibody levels and decreased IgE production. IgG are called “blocking antibody”. Sublingual immunotherapy (SLIT) with natural rubber latex (NRL) has recently been proposed and was safe and effective; no SLIT-related side effects had been observed. Bernardini et al. (2008a) used commercial latex SLIT in pediatric patients and observed the effect for three years. A significant reduction of the glove-use score was observed after 1, 2, and 3 years of treatment with SLIT. Baseline wheal areas of skin prick test and baseline values of serum specific IgE were significantly reduced. They concluded that three years of latex SLIT is safe, and it consolidates the efficacy of treatment in pediatric patients. In addition, current

subcutaneous immunotherapy schedules have been tested for treatment of latex allergy with evidence of efficacy, but the risks of adverse events have been high.
For such potent allergens as latex, hypoallergenic but T cell-reactive preparations are required for clinical use. For this, it is essential to identify allergenic components of latex products with generation of monoclonal antibodies and recombinant allergens, allowing sequence determination and mapping of T cell and B cell epitopes. Potential hypoallergenic latex preparations identified include modified non-IgE-reactive allergen molecules and short T cell epitope peptides. Together, these reagents and data should facilitate improved diagnostics and investigation of novel-specific therapeutics. The co-administration of adjunct therapies, such as anti-IgE or corticosteroids, and appropriate adjuvant for induction of regulatory T cell response offer promise for clinically effective, and development of safe latex-specific candidate vaccines.

12. Conclusion

Latex products have had many useful roles in the medical fields. Unfortunately the allergic responses to latex have become causes of both morbidity and mortality. Avoidance of exposure to allergen is essential to minimizing complications in patients suspected to be at risk, butthere is lack of information concerning latex allergen content of medical equipment leading to an increased risk to sensitized patients. Occupational health need to be a guideline and should be prepared for any emergency. Patients with well documented latex hypersensitivity can undergo surgical procedures with proper panning and care. Further strategies must be focused not only on the reduction of allergens during latex manufacture and development of suitable non-latex gloves, but also on the immunotherapy and development of vaccine.

13. References

Amarasekera, M., Rathnamalala, N., Samaraweera, S. & Jinadasa, M. (2010). Prevalence of latex allergy among healthcare workers. *Int J Occup Med Environ Health.*, Vol.23, No.4, (May-Jun 2010), pp.391-396, ISSN 1232-1087

Arellano, R., Bradley, J. & Sussman, G. (1992). Prevalence of the latex sensitization among hospital physicians occupationally exposed to latex gloves. *Anesthesiology*, Vol.77, No.5, (Nov 1992), pp.905-908, ISSN 0003-2999

Agarwal, S. & Gawkrodger, D.J. (2002). Latex allergy: a health care problem of epidemic proportions. *Eur J Dermatol.*, Vol.12, No.4, (Jul-Aug 2002), pp.311-315, ISSN 1167-1122

Armentia, A., Dueñas-Laita, A., Bartolomé, B., Martín-Gil, F.J., San Miguel, A. & Castrodeza, J.J. (2010). Clinical significance of cross-reactivity between tobacco and latex. *Allergol Immunopathol.*,Vol.38, No.4, (Jul-Aug 2010), pp.187-196, ISSN 0301-0546

Ausili, E., Tabacco, F., Focarelli, B., Nucera, E., Patriarca, G. & Rendeli, C. (2007). Prevalence of latex allergy in spina bifida: genetic and environmental risk factors. *Eur Rev Med Pharmacol Sci.*, Vol.11, No.3, (May-Jun 2007), pp.149-153, ISSN 1128-3602

Bains, S.N., Hamilton, R.G., Abouhassan, S., Lang, D., Han, Y., & Hsieh, F.H. (2010). Identification of clinically relevant cross-sensitization between *Soliadgo virgaurea* (Goldenrod) and *Hevea brasiliensis* (Natural Rubber Latex). *J Investig Allergol Clin Immunol.,* Vol.20, No.4, pp.331-339, ISSN 1018-9068

Barre, A., Culerrier, R., Granier, C., Selman, L., Peumans, W.J., Van Damme, E.J., Bienvenu, F., Bienvenu, J. & Rougé, P. (2009). Mapping of IgE-binding epitopes on the major latex allergen Hev b 2 and the cross-reacting 1,3beta-glucanase fruit allergens as a molecular basis for the latex-fruit syndrome. *Mol Immunol*., Vol.46, No.8-9, (May 2009), pp.1595-1604, ISSN 0161-5890

Bascom, R., Fisher J.F., Thomas, R.J., Yang, W.N., Baser, M.E. & Baker, J.H. (1988). Eosinophilia, respiratory symtoms, and pulmonary infiltrates in rubber workers. *Chest*. Vol.93, No.1, (Jan 1988), pp.154-158, ISSN 0012-3692

Baur, X., Chen, Z,. Rozynek, P., Duser, M. & Raulf-Heimsoth, M. (1995). Cross-reacting IgE antibodies recognizing latex allergens, including Hev b, as well as papain. *Allergy*, Vol. 50, No.7, (Jul 1995), pp. 604-609, ISSN 0105-4538

Belleri, L. & Crippa, M. (2008). Old and new types of sanitary gloves: what has improved? *Med Lav.*,Vol. 99, No.2, (Mar-Apr 2008), pp.80-84, ISSN 0025-7818

Bendewald, M.J., Farmer, S.A. & Davis, M.D. (2010). An 8-year retrospective review of patch testing with rubber allergens: the Mayo Clinic experience. *Dermatitis*,Vol.21, No.1, (Feb 2010), pp.33-40, ISSN 1710-3568

Bernardini, R., Pecora, S., Milani, M. & Burastero, S.E. (2008a). Natural rubber latex allergy in children: clinical and immunological effects of 3-years sublingual immunotherapy. *Eur Ann Allergy Clin Immunol*., Vol.40, No.4, (Dec 2008), pp.142-147, ISSN 1764-1489

Bernardini, R., Pucci, N., Azzari, C., Novembre, E., De Martino, M. & Milani, M. (2008b). Sensitivity and specificity of different skin prick tests with latex extracts in pediatric patients with suspected natural rubber latex allergy-a cohort study. *Pediatr Allergy Immunol*., Vol.19, No.4, (Jun 2008), pp.315-318, ISSN 0905-6157

Bernstein, D.I., Biagini, R.E., Karnani, R., Hamilton, R., Murphy, K., Bernstein, C., Arif S.A., Berendts, B. & Yeang, H.Y. (2003). *In vivo* sensitization to purified *Hevea brasiliensis* proteins in health care workers sensitized to natural rubber latex. *J Allergy Clin Immunol*., Vol.111, No.3, (Mar 2003), pp.610-616, ISSN 0091-6749

Beezhold, D.H., Hickey, V.L., Kostyal, D.A., Puhl, H., Zuidmeer, L., van Ree, R., Sussman, GL. (2003). Lipid transfer protein from Hevea brasiliensis (Hev b 12), a cross-reactive latex protein. *Ann Allergy Asthma Immunol.* Vol.90, No.4, (Apr 2003), pp.439-445, ISSN 1081-1206

Bousquet, J., Flahault, A., Vandenplas, O., Ameille, J., Duron, J.J., Pecquet, C., Chevrie, K. & Annesi-Maesano, I. (2006). Natural rubber latex allergy among health care workers: a systematic review of the evidence. *J Allergy Clin Immunol.,* Vol.118, No.2, (Aug 2006), pp.447-454, ISSN 0091-6749

Boxer, M.B., Grammer, L.C., Orfan, N. (1994). Gutta-percha allergy in a health care worker with latex allergy. *J Allergy Clin Immunol*., Vol.93, No.5, (May 1994), pp.943-944, ISSN 0091-6749

Brown, R.H., Hamilton, R.G., Mintz, M., Jedicka, A.E., Scott, A.L. & Kleeberger S.R. (2005). Genetic predisposition to latex allergy. Role of Interleukin 13 and Interleukin 18. *Anesthesiology*, Vol.102, No.3, (Mar 2005), pp.496-502, ISSN 0003-2999

Cao, L.Y., Taylor, J.S., Sood, A., Murray, D. & Siegel, P.D. (2010). Alergic contact dermatitis to synthetic rubber gloves: changing trends in patch test reactions to accelerators. *Arch Dermatol*., Vol.146, No.9, (Sep 2010), pp.1001-1007, ISSN 0003-987X

Charous, B.L., Hamilton, R.G. & Yonginger, J.W. (1994). Occupational latex exposure: characteristics of contact and systemic reactions in 47 Works. *J Allergy Clin Immunol*., Vol.94, No.1, (Jul 1994), pp.12-18, ISSN 0091-6749

Chen, Z., Cremer R, Posch, A., Raulf-Heimsoth, M., Rihs, H., Baur, X. (1997). On the allergenicity of Hev b 1 among health care workers and patients with spina bifida allergic to natural rubber latex. *J Allergy Clin Immunol*., Vol.100, No.5, (Nov 1997), pp.684-693, ISSN 0091-6749

Cleenewerck, M.B. (2010). Update on medical surgical gloves. *Eur J Dermatol.,* Vol.20, No.4, (Jul-Aug 2010), pp. 434-442, ISSN 1167-1122

Costa, G.E., Johnson, J.D. & Hamilton, R.G. (2001). Cross-reactivity studies of guttapercha, gutta-balata, and natural rubber latex (*Hevea brasiliensis*). *J Endod*., Vol. 27, No.9, (Sep 2001), pp.584-587, ISSN 0099-2399

Cremer, R. & Mennicken O. (2011). Longitudinal study on specific IgE against natural rubber latex, banana and kiwi in patients with spina bifida. *Klin Padiatr*., (Apr 2011). [Epub ahead of print], ISSN 1439-3824

Diéguez, M.C., Pulido, Z., de la Hoz, B., Blanco, R., Cerecedo, I., Fernández-Caldas, E. & Swanson, M. (2007). Latex allergy in healthcare workers: an epidemiological study in a Spanish hospital. *Allergy Asthma Proc*., Vol.28, No.5, (Sep-Oct 2007), pp.564-570, ISSN 1088-5412

Downing, J. (1993). Dermatitis from rubber gloves. *N Engl J Med*., Vol.208, (Jan 1993), pp.196-198, ISSN 0028-4793

Dyck, R.J. (2000). Historical development of latex allergy. *AORN J*., Vol.72, No.1, (Jul 2000), pp.27-40, ISSN 0001-2092

Ebo, D.G., Hagendorens, M.M., De Knop, K.J.,Verweij, M.M., Bridts, C.H., De Clerck, L.S. & Stevens, W.J. (2010). Component-resolved diagnosis from latex allergy by microarray. *Clin Exp Allergy,* Vol.40, No.2, (Feb 2010), pp.348-358, ISSN 0954-7894

Förström, L. (1980). Contact urticaria from latex surgical gloves. *Contact Dermatitis*, Vol.6, No.1, (Jan 1980), pp.33-34, ISSN 0105-1873

Hamann, C.P., Rodgers, P.A. & Sullivan, K.M. (2005). Prevalence of type I natural rubber latex allergy among dental hygienists. *J Dent Hyg*., Vol.79, No.2, (Apr 205), pp.7, ISSN 1043-254X

Hamann, C.P., Turjanmaa, K., Rietschel, R., Siew, C., Owensby, D., Gruning,er S.E. & Sullivan K.M. (1998). Natural Rubber Latex Hypersensitivity: Incidence and Prevalence of Type I Allergy in the Dental Professional. *JADA*, Vol.129, No.1, (Jan 1998), pp.43-54, ISSN 0002-8177

Heitz, J.W. & Bader, S.O. (2010). An evidence-based approach to medication preparation for the surgical patient at risk for latex allergy: is it time to stop being stopper poppers? *J Clin Anesth.,* Vol.22, No.6, (Sep 2010), pp.477-83, ISSN 0952-8180

Kelly, K.J., Setlock, M. & Davis, J.P. (1991). Anaphylactic reactions during general anesthesia among pediatric patients. *MMWR,* Vol.40, No.26, (Jul 1991), pp.437-443, ISSN 0149-2195

Kosti, E. & Lambrianidis, T. (2002). Endodontic treatment in cases of allergic reaction to rubber dam. *J. Endod*., Vol.28, No.11, (Nov 2002), pp.787-789, ISSN 0099-2399

Lin, C.T., Hung, D.Z., Chen, D.Y., Wu, H.J., Lan, J.L. & Chen, Y.H. (2008). A hospital-based screening study of latex allergy and latex sensitization among medical workers in Taiwan. *J Microbiol Immunol Infect*., Vol.41, No.6, (Dec 2008), pp.499-506, ISSN 1684-1182

Machado, J.A., da Cunha, R.C., de Oliveira, B.H. & da Silva, J. (2011). Latex-induced anaphylactic reaction in a patient undergoing open appendectomy. Case report. *Rev Bras Anestesiol.*, Vol.61, No. 3, (May-Jun 2011), pp.360-366, ISSN 0034-7094

Malerich, P.G., Wilson, M.L. & Mowad, C.M. (2008). The effect of a transition to powder-free latex gloves on workers' compensation claims for latex-related illness. *Dermatitis*, Vol.19, No.6, (Nov-Dec 2008), pp.316-318, ISSN 1710-3568

Mebra, P. & Hunter, M.J. (1998). Latex allergy: a review of considerations for the oral and maxillofacial surgeon. *J Oral Maxillofac Surg.,* Vol.56, No.12, (Dec 1998), pp.1426-1430, ISSN 0278-2391

Monitto, C.L., Hamilton, R.G., Levey, E., Jedlicka, A.E., Dziedzic, A., Gearhart, J.P., Boyadjiev, S.A. & Brown, R.H. (2010). Genetic predisposition to natural rubber latex allergy differs between health care workers and high-risk patients. *Anesth Analg*., Vol.110, No.5, (May 2010), pp.1310-1317, ISSN 0003-2999

Nabavizadeh, S.H., Anushiravani, A. & Amin, R. (2009). Natural rubber latex hypersensitiveity with skin prick test in operating room personnel. *Iran J Allergy Asthma Immunol*., Vol.8, No.4, (Dec 2009), pp.219-20, ISSN 1735-1502

Nettis, E., Di Leo, E., Calogiuri, G., Milani, M., Donne, PD., Ferrannini, A. & Vacca, A. (2010). The safety of a novel sublingual rush induction phase for latex desensitization. *Curr Med Res Opin*., Vol.26, No.8, (Aug 2010), pp.1855-1859, ISSN 0300-7995

Nettis, E., Assennato, G., Ferrannini, A. & Tursi, A. (2002). Type I allergy to natural rubber latex and type IV allergy to rubber chemicals in health care workers with glove-related skin symptoms. *Clin Exp Allergy,* Vol.32, No.3, (Mar 2002), pp.441-447, ISSN 0954-7894

Nieto, A., Mazón, A., Boquete, M., Carballada, F., Asturias, J.A., Martínez, J., Martínez, A. (2002). Assessment of profilin as an allergen for latex-sensitized patients. *Allergy*, Vol.57, No.9, (Sep 2002), pp.776-784, ISSN 0105-453

Nolte, H., Babakhin, A., Babanin, A., Bakhutashvili, V., Beloglazov, V., Bezruchenko, O., Blaziene, A., Chuchalin, A., Drannik, G., Endre, L., Khaitov, R., Khanferyan, R., Kowal, K., Kowalski, M., Markov, A., Petrov, R., Puchlik, B., Rosovenko, A., Sepiashvili R., Stepka, K., Titov, L., Tsybulkina, V., Yashina, L., Zakirova, I. & DuBuske, L.M. (2002). Prevalence of skin teste reactions to natural rubber latex in hospital personnel in Russia and Eastern Europe. *Annals of Allergy, Asthma & Immunology*, Vol.89. No.5, (Nov 2002), pp.452-456, ISSN 1081-1206

Nutter, A.F. (1979). Contact urticaria to rubber. *Br J Dermatol*., Vol.101, No.5, (Nov 1979), pp.597-598, ISSN 0007-0963

Ott, H., Schröder, C., Raulf-Heimsoth, M., Mahler, V., Ocklenburg, C., Merk, H.F. & Baron, J.M. (2010). Microarrays of Recombinant *Hevea brasiliensis* Proteins: A novel tool for the component-resolved diagnosis of natural rubber latex allergy. *J Investig Allergol Clin Immunol.,* Vol.20, No.2, pp.129-138, ISSN 1018-9068

Ownby, D.R., Ownby, H.E., McCullough, J.A. & Shafer, A.W. (1994). The prevalence of anti-latex antibodies in 1000 volunteer blood donors. *J Allergy Clin Immunol*., Vol.97, No.6, (Jun 1994), pp.1188-1192, ISSN 0091-6749

Ownby, D.R. (2002). A history of latex allergy. *J Allergy Clin Immunol*., Vol.110, (Aug 2002), pp.S27-32, ISSN 0091-6749

Pedraza-Escalona, M., Becerril-Luján, B., Agundis, C., Domínguez-Ramírez, L., Pereyra, A. Riaño-Umbarila, L. & Rodríguez-Romero, A. (2009). Analysis of B-cell epitopes

from the allergen Hev b 6.02 revealed by using blocking antibodies. *Mol Immunol.*, Vol.46, No.4, (Feb 2009), pp.668-676, ISSN 0161-5890

Peixinho, C., Tavares-Ratado, P., Tomás, M.R., Taborda-Barata, L. & Tomaz, C.T. (2008). Latex allergy: new insights to explain different sensitization profiles in different risk groups. *Br J Dermatol.*, Vol.159, No.1, (Jul 2008), pp.132-136, ISSN 0007-0963

Perkin, J.E. (2000). The latex and food allergy connection. *J Am Diet Assoc.*, Vol.100, No. 11, (Nov 2000), p.1381-1384, ISSN 0002-8223

Radauer, C., Adhami, F., Fürtler, I., Wagner, S., Allwardt, D., Scala, E., Ebner, C., Hafner, C., Hemmer, W., Mari, A. & Breiteneder, H. (2011). Latex-allergic patients sensitized to the major allergen hevein and hevein-like domains of class I chitinases show no increased frequency of latex-associated plant food allergy. *Mol Immunol.*, Vol.48, No.4, (Jan 2011), pp.600–609, ISSN 0161-5890

Rihs, H.P., Chen, Z., Rozynek, P., Cremer, R. (2001). Allergenicity of rHev b 10 (manganese-superoxide dismutase). *Allergy*, Vol.56, No.1, (Jan 2001), pp.85-86, ISSN 0105-4538

Rihs, H-P., Chen, Z., Ruëff, F., Cremer, R., Raulf-Heimsoth, M., Baur, X., Moneret-Valtrin, D.A. & Brüning, T. (2002). 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.*, Vol.110, No.3, (Sep 2002), pp.507-514, ISSN 0091-6749

Rolland, J.M. & O'Hehir, R.E. (2008). Latex allergy: a model for therapy. *Clin Exp Allergy,* Vol.38, No.6, (Jun 2008), pp.898-912, ISSN 0954-7894

Rougé, P., Culerrier, R., Campistron, M., Granier, C., Bienvenu, F., Bienvenu, J., Didier, A. & Barre, A. (2010). Allergenicity of Hev b 13, a major esterase allergen in natural rubber latex (*Hevea brasiliensis*) allergy, does not only depend on its carbohydrate moiety. *Mol Immunol.*, Vol.47, No.4, (Jan 2010), pp.871-7, ISSN 0161-5890

Sekiya, K., Watai, K., Taniguchi, M., Mitsui, C., Fukutomi, Y., Tanimoto, H., Kawaura, N., Akiyama, K. (2011). Latex Anaphylaxis caused by a Swan-Ganz catheter. *Intern Med.*, Vol.50, No.4, (Feb 2011), pp.355-357, ISSN 18410987

Slater, J.E., Vedvick, T., Arthur-Smith, A., Trybul, D.E. Kekwick, R.G.O. (1996). Identification, Cloning, and Sequence of a Major Allergen (Hev b 5) from Natural Rubber Latex (*Hevea brasiliensis*). *The Journal of Biological Chemistry*, Vol.271, No.41, (October 1996), pp. 25394–25399, ISSN 0021-9258

Smith, A.M., Amin, H.S., Biagini, R.E., Hamilton, R.G., Arif, S.A., Yeang, H.Y. & Bernstein, D.I. (2007). Percutaneous reactivity to natural rubber latex proteins persists in health-care workers following avoidance of natural rubber latex. *Clin Exp Allergy,* Vol.37, No.9, (Sep 2007), pp.1349-56, ISSN 0954-7894

Sonofuchi, K., Watanabe, K., Onuma, T., Kaneko, T., Ohmizo, H., Furuta, S., Endo, K. & Morota, T. (2010). A case of anaphylactic shock by multiple causes. *Masui-The Japanese Journal of anesthesiology,* Vol.59, No.8, (Aug 2010), pp.1032-1035, ISSN 0021-4892

Sripaiboonkij, P., Phanprasit, W. & Jaakkola, M.S. (2009). Respiratory and skin effects of exposure to wood dust from the rubber tree *Hevea brasiliensis*. *Occup Environ Med.*, Vol.66, No.7, (Jul 2009), pp.442-447, ISSN 1351-0711

Sukekava, F. & Sell, A.M. (2007). Rubber latex gloves hypersensitivities in dental workers. *Acta Sci. Health Sci.*, Vol.29, No.1, (Jan-Jun, 2007), pp.39-44, ISSN 1679-9291.

Sussman, G.L. & Beezold, D.H. (1994). Latex allergy– a clinical perspective. *J Long-Term Effects Med Implants*, Vol.4, No.2-3, (Jul 1994), pp.95-110, ISSN 1050-6934

Turillazzi, E., Greco, P., Neri, M., Pomara, C. Riezzo, I. & Fineschi, V. (2008). Anaphylactic latex reaction during anesthesia: the silent culprit in a fatal case. *Forensic Sci Int.*, Vol.179, No.1, (Jul 2008), pp.5-8, ISSN 0379-0738

Turjanmaa, K., Kanto, M. Kautiainen, H., Reunala, T., Palosuo, T. (2002). Long-term outcome of 160 adult patients with natural rubber latex allergy. *J Allergy Clin Immunol.,* Vol.110, (Aug 2002), pp.S70-4, ISSN 0091-6749

Turjanmaa, K. (1987). Incidence of immediate alergy to latex gloves in hospital personnel. *Contact Dermatitis*, Vol.17, No.5, (Nov 1987), p.270-275, ISSN 0105-1873

Ueda, N., Kitamura, R., Wakamori, T., Nakamura, K., Konishi, K. (2008). Anaphylactic reaction to latex during spinal anesthesia: a case report. *Masui-The Japanese Journal of anesthesiology,* Vol.57, No.5, (May 2008), pp.637-639, ISSN 0021-4892

Unsel, M., Mete, N., Ardeniz, O., Göksel, S., Ersoy, R., Sin, A., Gulbahar, O. & Kokuludag, A. (2009). The importance of nasal provocation test in the diagnosis of natural rubber latex allergy. *Allergy*, Vol.64, No.6, (Jun 2009), pp.862-867, ISSN 0105-4538

van Kampen, V., Raulf-Heimsoth, M., Sander, I. & Merget, R. (2010). Diagnostics of occupational type I allergies-comparison of skin prick test solutions from different manufacturers for selected occupational allergens. *Pneumologie*., Vol.64, No.5, (May 2010), pp.271-277, ISSN 0033-4073

Verdolin, B.A., Villlas Boas, W.V. & Gomez, R.S. (2003). Latex Allergy: accidental diagnosis after urological procedure. Case Report. *Rev. Bras. Anestesiol.*, Vol.53, No.4, (Aug 2003), pp.496-500, ISSN 0034-7094

Wagner, S. & Breiteneder, H. (2002). The latex-fruit syndrome. *Biochem Soc Trans.,* Vol.30, No.6, (Nov 2002), pp.935-940, ISSN 0300-5127

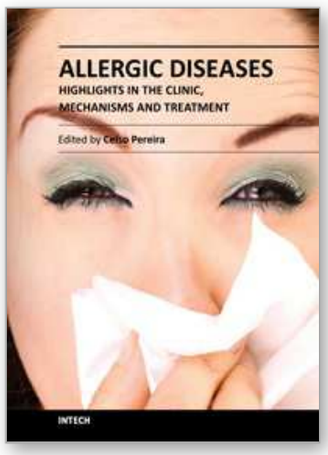
Wagner, B., Krebitz., M, Buck, D., Niggemann, B., Yeang, H.Y., Han, K.H., Scheiner, O. & Breiteneder H. (1999). Cloning, expression, and characterization of recombinant Hev b 3, a *Hevea brasiliensis* protein associated with latex allergy in patients with spina bifida. *J Allergy Clin Immunol.,* Vol.104, No.5, (Nov 1999), pp.1084-1092, ISSN 0091-6749

Wagner, S., Breiteneder, H., Simon-Nobbe, B., Susani, M., Krebitz, M., Niggemann, B., Brehler, R., Scheiner, O., Hoffmann-Sommergruber, K. (2000). Hev b 9, an enolase and a new cross-reactive allergen from hevea latex and molds. Purification, characterization, cloning and expression. *Eur J Biochem*., Vol.267, No.24, (Dec 2000), pp.7006-7014, ISSN 0014-2956

Woods, J.A., Lambert, S., Platts-Mills, T.A.E., Drake, D.B. & Edlich, R. (1997). Natural rubber latex allergy: spectrum, diagnostic approach, and therapy. *The Journal of Emergency Medicine,* Vol.15, No.1, (Jan-Feb 1997), p.71-85, ISSN 0736-4679

Yagami, T., Osuna, H., Kouno, M., Haishima, Y., Nakamura, A., Ikezawa, Z. (2002). Significance of carbohydrate epitopes in a latex allergen with beta-1,3-glucanase activity. *Int Arch Allergy Immunol.,* Vol.129, No.1, (Sep 2002), pp.27-37, ISSN 1018-2438

Yeang, H.Y., Cheong, K.F., Sunderasan, E., Hamzah, S., Chew, N.P., Hamid, S. Hamilton R.G., Cardosa, M.J. (1996). The 14.6 kD (Hev b3) rubber particle proteins are recognized by IgE from spina bifida patients with allergy. *J Allergy Clin Immunol.,* Vol.98, No.3, (Sep 1996), pp.628-639, ISSN 0091-6749



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The present Edition "Allergic diseases - highlights in the clinic, mechanisms and treatment" aims to present some recent aspects related to one of the most prevalent daily clinical expression disease. The effort of a group of outstanding experts from many countries reflects a set of scientific studies very promising for a better clinical care and also to the treatment and control of the allergy. This book provides a valuable reference text in several topics of the clinical allergy and basic issues related to the immune system response. The inflammatory reaction understanding in allergic disease is clearly evidenced, as well as new strategies for further researches.

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