

Primary prevention of latex allergy in healthcare – spectrum of strategies including the European glove standardization

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doi:10.1111/j.1600-0536.2012.02057.x

Summary

IgE-mediated allergy to natural rubber latex was first noted from rubber gloves in 1979. The initial reports in dermatological journals described contact urticarial reactions; later, severe generalized allergic reactions and asthma were documented. A considerable proportion of the people involved in medical and dental care were found to be sensitized to latex. This article describes and surveys a broad range of primary prevention measures at the local and national levels. Examples are given from paediatrics, dental education, and medical care. National strategies and position papers on latex allergy are presented in which medical professionals, manufacturers and public authorities have cooperated. Special reference is paid to the European work to standardize medical gloves, which led to document EN 455:3.

Key words: CEN; medical care; natural rubber; protection.

In the past few decades, latex allergy has been recognized as a considerable risk factor for severe generalized allergic reactions and occupational asthma, mainly in medical and dental care (1–4). Among dermatologists, this IgE-mediated allergy to natural rubber latex is a well-known cause of allergic contact urticaria (5). The offending allergens are proteins from the sap of the rubber tree *Hevea brasiliensis* that persist in manufactured natural rubber latex products. The word latex is ambiguous, but in this article it is used synonymously with natural rubber latex. To illuminate various aspects of the prevention of this allergy, we have surveyed scientific publications and documents from public authorities.

Natural rubber latex is the traditional material in medical gloves. The British dermatologist Nutter wrote the first report on contact urticaria provoked by rubber gloves, published in 1979 (6). Initially, latex allergy was mainly recognized in Europe (6–12), but it soon attracted

attention worldwide (13–15). The recognition of latex allergy during the 1980s coincided with a steep increase in the use of powdered latex gloves in healthcare, as a part of viral infection control programmes. Re-use and washing of surgical gloves also ceased. Numerous case reports and reviews have documented the clinical picture, varying from localized contact urticaria (Fig. 1) to life-threatening anaphylactic reactions. In 1999, Kujala surveyed epidemiological studies on latex allergy among healthcare workers, and found the following prevalence rates: operating room staff, 5–16%; dental staff, 2–38%; physicians, 1–10%; nurses, 1–22%; and technicians, 1–17% (16). In a literature survey in 2002, Charous et al. found the prevalence of occupational asthma to be 2–10% in highly exposed workers (17). Other occupational groups that use protective gloves and in whom latex allergy is recognized include, for example, food handlers (18). Diagnostic tools have been developed and evaluated (19–22), major allergens have been identified (23), and allergen levels in products made from natural rubber latex have been measured, with immunological methods (24, 25).

The allergen content in latex products varies, partly depending on how they have been manufactured (25, 26). Enhanced leaching during the manufacturing process

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Accepted for publication 29 October 2011



Fig. 1. Contact urticaria provoked by a latex glove.

is the main method used to reduce the water-soluble allergen content. To prevent stickiness, the surface of latex gloves is powdered with corn starch, and during manufacture the glove powder is contaminated with latex allergens (27). Such contaminated glove powder contributes to airborne latex allergen exposure. The development of powder-free latex products has been of crucial importance in allergy prevention. Manufacturing powder-free gloves involves etching the latex surface and more rinsing steps; such gloves tend to have a lower allergen content than powdered gloves (25), and airborne allergen spread is prevented.

Initiatives to prevent latex allergy have been taken at the local, national and international levels; physicians, researchers and public authorities have cooperated with manufacturers of latex products. The main preventive measures have been to switch from powdered to powder-free latex gloves and to latex-free alternatives. Such preventive initiatives have borne fruit not only locally, but also at the national level, with positive trends being reported in Finland, Germany, and Belgium (28–32).

The aim of the present study was to survey the wide range of measures used to prevent latex allergy that have been presented in the scientific literature and to stimulate interest in dermatology for continued preventive work. The intention is not to give an exhaustive literature review, but to exemplify the diversity of preventive initiatives. Special attention is paid to the European glove standardization work.

Methods

To give a picture of latex allergy prevention, publications presenting preventive strategies were surveyed. Both review articles and original articles were scrutinized. The literature selection was based on a search in PubMed for latex allergy or natural rubber latex allergy in combination with other keywords; prevention, primary prevention, position paper, and preventive strategies. The work of the European standardization committee (CEN) was also studied, particularly the CEN standard EN 455:3 on medical gloves for single use, and additional European policy documents. Local, national and European perspectives are presented separately.

Examples of Local Strategies

The scientific literature contains many descriptions of local measures used to prevent latex allergy.

Paediatrics

Early on, paediatricians drew attention to the high prevalence of latex allergy among children with spina bifida and children who underwent multiple surgical interventions at a young age. In 1994, the Children's Hospital of La Fe in Valencia, Spain, implemented a latex-free environment in wards where children with spina bifida were treated. After this, the prevalence of latex sensitization among those children fell from 26.7% to 4.5% (33). From Germany, Cremer et al. reported that, when a latex-free operating theatre was established at Cologne's Children's Hospital in 1995, the proportion of patients with spina bifida who were sensitized to latex allergens fell from 42% to 7% (34). After three severe anaphylactic reactions (one of which was fatal), the Paediatric Surgical Hospital in Lyon, France successively implemented a complete latex avoidance policy in the operating theatre and perioperative-care area, and since 2002, no latex-related anaphylaxis has been recorded (35). The Spina Bifida Association provides information on latex-containing articles and latex-free alternatives for use in hospital environments (36).

Dental education

Several latex allergy prevention programmes in dental schools have been documented. In 1999, Levy et al. described a study performed at two dental schools, one in Paris and one in London. In summary, 11/96 students who had used powdered, protein-rich latex gloves were sensitized to latex, as compared with 0/93 who had used powder-free protein-poor latex gloves (37). The latex

sensitivity of students at the dental school in Toronto, Canada was studied in 1995 and 2000. From 1995 onwards, the school had purchased low-protein, non-powdered latex gloves. Latex prick test positivity among comparable groups of students changed from 10% in 1995 to 3% in 2000 (38). At Cardiff dental school, powdered latex gloves were replaced in 1997 by non-powdered latex gloves. Dental students were thereafter followed in a longitudinal study that included prick testing. No student developed latex sensitivity during a 5-year follow-up period (39).

Medical care

Healthcare institutions in several countries have documented programmes for primary and secondary prevention. In papers from 1994 and 2001, Tarlo et al. in Canada stated that use of powder-free latex gloves by co-workers of a sensitized laboratory technician enabled her to continue work with own latex avoidance, and also prevented measurable airborne latex allergen exposure (40). A control programme including education and conversion to low-protein, powder-free latex gloves in an Ontario teaching hospital resulted in a fall in the number of latex allergy cases (41). The positive effect of such glove conversion on the possibility of continuing at work was also documented by Allmers et al. 1998 in Germany, who recommended the banning of powdered latex gloves in the workplace and a supply of latex-free materials for sensitized individuals (42). The use of non-latex or low-allergenic gloves in healthcare was recommended by Turjanmaa in Finland 2002 in a long-term outcome study of 160 latex-allergic patients (43). Filon et al. reported from Trieste Hospital in Italy that all powdered latex gloves were replaced by low-protein powder-free alternatives as of 1999–2000. In 1997, 9.6% of the personnel were positive to latex; at follow-up in 2000–2002, none of the personnel with newly reported glove intolerance were diagnosed as allergic to latex. However, personnel who had already become sensitized to latex had to use latex-free gloves to avoid symptoms (44). An example of secondary prevention was reported in 2000 from the University Hospital in Aichi, Japan. Information seminars on latex allergy were held at the dental centre and emergency and operating rooms, in conjunction with a change from powdered to powder-free latex or non-latex gloves. These steps, together with individual latex avoidance, resulted in successful secondary prevention in 16 latex-sensitized staff members (45). At Geisinger Medical Center in Danville, PA, United States, the number of workers' compensation claims for latex-related illness decreased significantly after transition from powdered to powder-free latex gloves (46).

Table 1. Position papers on latex allergy by medical associations

UK

- Latex allergy. A position paper of the British Society of Allergy and Clinical Immunology (2003) (50)
- Latex allergy, occupational aspects of management. A national guideline. Royal College of Physicians (2008) (51)

United States

- Guidelines for the management of latex allergies and safe latex use in health care facilities. American College of Allergy, Asthma & Immunology ACAAI (1996) (52)
- American Academy of Dermatology's position paper on latex allergy (1998) (53)
- American Nurses Association. Position statement on latex allergy (1998) (54)

Australia, Asia

- Guidelines for hospital management of latex allergic patients. The Australasian Society of Clinical Immunology and Allergy (updated 2010) (55)

Examples of National Strategies

In addition to the local initiatives, national authorities have been active in the preventive work.

In Germany, the Technical Regulation for Dangerous Substances (TRGS) classifies natural rubber latex as a sensitizer in TRGS 907/2002. TRGS 401/2008 stipulates that latex gloves for single use that are used for hygienic purpose should be powder-free (47). In the UK, information from the Health and Safety Executive gives advice on the selection of single-use gloves, particularly for healthcare workers and patients (48). In the United States, the National Institute for Occupational Safety and Health has published an alert on preventing allergic reactions to latex in the workplace (49).

Several medical associations have presented comprehensive compilations of current knowledge in national position papers and guidelines; see Table 1 (50–55).

In Finland, regular surveys of allergen content in medical gloves are performed. The decreasing incidence of latex allergy in healthcare personnel parallels a decreasing percentage of highly allergenic latex gloves (24, 28, 56).

Standards on Medical Gloves – European Perspective

The main risks for severe allergic reactions are seen in medical care and surgery, where latex-containing gloves and devices are in contact with skin, mucous membranes, and exposed tissue. Latex-containing devices include, for example, catheters, balloon cuffs, and dental cofferdams. As contact with latex gloves is the main cause of the latex allergic reactions in healthcare, special attention is paid to the standards for medical gloves in this article.

Table 2. European documents on natural rubber latex allergy and medical devices

- European Standard EN 455:3, Medical gloves for single use – Part 3: Requirements and testing for biological evaluation (2006) (57)
- Opinion on natural latex allergy adopted by the European Commission, Scientific committee on medicinal products and medical devices (2000) (58)
- Implications of the medical devices directives (93/42/EEC) in relation to medical devices containing natural rubber latex. A guide for manufacturers and notified bodies (2004) (59)
- Guidelines on medical devices. Clinical evaluation: a guide for manufacturers and notified bodies (2009) (60)

The International Organization for Standardization (ISO) has organized standards for medical gloves in categories based on the materials from which the gloves are made. Medical gloves made from natural rubber latex are regulated by ISO 12243:2003. Complementary to and parallel with the ISO standards, standards for single-use medical gloves made of various materials have been developed in Europe and the United States to give guidelines both for manufacturers and for purchasers of gloves.

European documents on latex allergy and medical devices are shown in Table 2 (57–60).

The European standards are prepared in cooperation with manufacturers, consumers, and experts from different fields. Each standard is formulated and revised in an ongoing process whereby new knowledge can be incorporated. The national standardization bodies in the EU countries nominate members to participate and decide on approval of the standard. The quality of a standard thus depends on the human, technical and economic resources in the group. The members of the working group represent interests from consumers, medical professionals, researchers, and manufacturers, all of whom contribute their knowledge. Scandinavian dermatologists were active at an early stage in the standardization work. One main issue during the preparation of the standard EN 455:3 was to harmonize existing methods of measuring proteins in latex gloves (61).

The European standard EN 455:3, *Medical gloves for single use – Part 3: Requirements and testing for biological evaluation*, was prepared under a mandate given in 1993 to CEN by the European Commission and the European Free Trade Association. It was approved in 1999 and updated in 2006. The scope of EN 455:3 is to specify requirements for biological safety of medical gloves, by stipulating labelling and test methods. The requirements in EN 455:3 concerning labelling of medical gloves are summarized in Table 3. Further questions dealt with in EN 455:3 are the presence of endotoxins, glove chemicals,

Table 3. Labelling requirements for medical gloves for single use in the European standard for medical gloves EN 455: part 3 (outlines)

- Gloves containing natural rubber latex shall be labelled on the packaging with a latex symbol, with an attached allergy warning text
- Glove labelling supposing low amounts of latex allergens shall be avoided
- The labelling shall indicate if the gloves are powder-free or powdered
- If the protein content is labelled, the process limit shall be presented
- Glove labelling shall not include any term suggesting relative safety

and powder. For gloves to be labelled as 'powder-free', the powder content should not exceed 2 mg per glove. In a normative annex, the test method for extractable proteins is presented – a modified Lowry assay. The leachable latex proteins in gloves shall be as 'low as reasonably practical', and no definitive limit has been defined. The manufacturers shall monitor the protein measuring test process, and have the test results available on request. There is no reliable correlation between the total protein content and the amounts of latex allergens in gloves (62). This has actualized the question of specific allergen measurements (63).

The national standard organizations in Europe are bound to implement the European standards. The full text of the standards can be purchased from the national standardization organizations.

Economic aspects

To meet the demand for less allergenic medical gloves, the market has now responded by supplying a greater selection of powder-free, low-protein medical latex gloves and also latex-free alternatives. Gloves made from synthetic rubber, such as nitrile, isoprene, and neoprene, and several plastic materials, such as polyurethanes and polyvinyl, are available. Attempts have been made to replace the latex proteins with casein from cow's milk (64) and to reduce the amount of latex proteins by enzymatic treatment (65); however, these methods may carry a risk of introducing further allergens into the manufacturing process. The cost of the switch to less allergenic but more expensive medical gloves has been estimated to be economically defensible, due to decreases in compensation claims and time lost from work (30, 41, 46, 66).

Discussion

In this literature survey on latex allergy, several successful preventive initiatives have been identified. The scientific reports confirm the positive preventive effect for medical personnel of switching from powdered to powder-free latex gloves or latex-free alternatives in medical and dental care (28–46). Decreases in the incidence of occupational

latex allergy have been reported from Finland, Germany, and Belgium (28, 29, 31). Regarding primary prevention for certain patient risk groups, for example children with spina bifida, strict latex-free environments have been created in paediatric care (33–35, 67). However, primary preventive measures do not imply that secondary preventive steps can be neglected for already sensitized persons (68). Latex-sensitized individuals thus still need their own latex avoidance measures.

Teamwork between researchers, clinicians and national authorities is reflected in the scientific literature. International cooperation and interdisciplinary collaboration between medical specialties also appear to be advantageous. The current CEN standard on medical gloves is an example of fruitful cooperation between medical professionals, scientists and manufacturers that facilitates the glove selection process. At a national level in Europe, there are encouraging reports from Germany, Belgium, and Finland (28–31). The interplay between medical professionals and public authorities has been important in decreasing the number of compensation claims resulting from latex-induced skin conditions, as pointed out in a study from Germany (30).

The wide interest in latex allergy is obvious from the multiplicity of scientific contributions from different medical fields. From a dermatological point of view, it is important to recognize and diagnose the contact urticarial response to latex materials in contact with the skin and mucous membranes, so as to give the necessary advice on prevention. Occupational dermatologists see glove intolerance reactions frequently. The diagnosis of allergic contact urticaria caused by latex is important. The diagnosis may be difficult to differentiate from glove-provoked dermatographism (69), unspecific

itch, skin irritation, and contact eczema caused by gloves.

IgE-mediated allergy is usually elicited by polypeptides and proteins derived from the vegetable and animal kingdoms (5). The latex allergens are organic polypeptides found in the sap of the rubber tree, but in healthcare it is not the contact with native latex that sensitizes, but rather contact with industrially manufactured products. Efforts to prevent latex allergy will thus be comparable to the measures used to reduce workers' and consumers' exposure to skin-sensitizing chemicals and products. Examples are: national workplace regulations concerning thermosetting plastics in some countries; the EU Cosmetics Directive, limiting some sensitizing chemicals, such as preservatives and hair dye substances; and REACH (Registration, Evaluation, Authorization and Restriction of Chemicals), which limits nickel release from items in direct and prolonged contact with the skin (formerly the Nickel Directive) (70).

Even though the prevalence of latex allergy in medical care shows a declining trend, continuous attention to allergy prevention is important to maintain the progress achieved. Researchers with clinical and theoretical expertise must still be able to participate in the work of CEN and in the work of national and international authorities to update regulations and recommendations.

Acknowledgements

We thank Christa Ahlenblom, Swedish Standards Institute, for valuable comments on the manuscript. The work was supported by grants from the Swedish Asthma and Allergy Associations Research Foundation, the Welander/Finsen Foundation, and the Swedish Council for Working Life and Social Research.

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