

Editorial

Diagnosis of latex allergy

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Allergy to natural rubber latex (NRL) has been known for more than 20 years. Although basically a normal IgE-mediated allergy to plant proteins from the rubber tree *Hevea brasiliensis* with cross-reactivity to other plant derivatives, and known as the latex-fruit syndrome, it has certain special features. Not only can sensitized patients react to NRL products, but they can also cause symptoms in other sensitized persons, as by touching with gloved hands. This has proved to be a problem especially in health care. In addition, airborne glove powder-bound latex allergens may cause symptoms in allergic persons (1–4).

In spite of many position papers and other recommendations, there is no consensus on how to diagnose allergy to NRL (5, 6). Even the criteria employed for positivity and negativity of tests are not uniform, although, at least in Europe, clear guidelines have been issued by the European Academy of Allergology and Clinical Immunology (EAACI) (7). This has led to many controversies in scientific papers and confusion among doctors and nurses not experienced in allergic diseases. Comparison of published results is often impossible.

The skin prick test (SPT) is the most reliable method of diagnosing sensitization to NRL, although the reproducibility of the test depends on many factors, some of which are difficult to standardize (8). So far only one standardized SPT allergen is available commercially (9). Among the unstandardized preparations, there is a test preparation kit which is available in three different concentrations. Unfortunately, the sensitivities and specificities are not given for any of them, and investigators seldom mention which concentration has caused the positive reaction. Glove eluates in 1:5 w/v have been used for years as the preferred method for diagnosing sensitization to NRL (3). In most papers, the glove

used is not specified, not to mention the allergenicity or lot number. Today, when gloves have become less allergenic, finding a reliable test glove is difficult (10). The use of diluted latex milk has proved to be dangerous. There are reports of anaphylactic reactions in Europe (11), and, in the USA, the use of self-made latex dilutions in prick testing has led to fear of *in vivo* diagnostics. There is still no commercially available SPT preparation (12). When unstandardized preparations are used, the researchers should first do a study to compare their SPT materials with those available on the market and with challenge tests (13).

RAST and AlaSTAT are the most commonly used *in vitro* tests for diagnosis of sensitization to NRL (4). They are less sensitive than the SPT but can safely be used also by doctors not familiar with the SPT. Low concentrations of specific IgE may appear because of cross-allergenicity to different fruits and vegetables (14). However, anaphylactic intraoperative reactions have been reported in latex SPT-positive but RAST-negative patients (15).

The atopy patch test (APT) has proved to be useful in studying eczematous skin reactions to aeroallergens in atopic patients. In most cases, the SPT and APT show positivity at the same time, but in some patients with no specific IgE to the allergen studied, only a positive APT reaction was verified (16). Similarly, Wilkinson & Beck reported positive patch test reactions to latex in glove-using patients with hand dermatitis with or without concomitant contact urticaria (17). They recommend routine use of latex in patch test series when testing glove-using patients with hand dermatitis. However, standardization of the test material and interpretation of test reactions should be defined before it is adopted for routine use, because the latex patch test caused an anaphylactic reaction in one latex SPT-positive patient (18).

The only reliable diagnostic method of verifying allergy is the challenge or provocation test. The glove challenge has been thoroughly described (19), but, again, the reduced allergenicity of gloves and the difficulty of obtaining reliable information about it diminishes the usefulness of this test. In the paper by Ruëff et al. (26) in this issue of *Allergy*, a powdered Sempermed glove was used. In the list of the National Agency for Medicines, four different Sempermed gloves were studied, and they varied widely in allergenicity (20). A commercially available latex sheet specially made for skin challenge tests and with given allergenicity is highly desirable. The same standardized material could be used for the lung and nose provocation tests that are needed when there are respiratory symptoms, especially when an occupational disease is suspected (21). Even the criteria for positivity of a challenge test are not uniform (22). I have encountered several patients who showed a negative reaction to a challenge test with a finger piece of a glove known to be highly allergenic, but who were positive to a whole hand challenge. Even several hours was needed to provoke symptoms in two patients with intact skin (19). In the paper by Ruëff et al. (26) in this issue, itching and redness are used as positive criteria for latex allergy, but these are difficult to interpret, and a real urticarial reaction should be required.

The terms "sensitization" and "allergy" are also widely confused, but the EAACI Nomenclature Task Force is now revising the terminology of allergology (S. G. O. Johansson, personal communication). The paper by Ylitalo et al. (23) clearly shows that the challenge test was positive in several patients with positive SPT and specific IgE antibodies to NRL but without any known symptoms connected to the use of NRL products. In the paper by Ruëff et al. (26) also, one of four NRL-allergic persons had no previously known symptoms. If no appropriate challenge test is performed, we should not speak about "only" sensitization. On the other hand, small SPT reactions, i.e., mean diameter of < 3 mm, as in the paper by Ruëff et al. (26), may be due to cross-reactivity to fruits and vegetables, and may not have anything to do with sensitization to NRL. According to Dreborg et al., SPT reactions of less than 3 mm in diameter are not reliable as indicators of sensitization (24). Hadjiliadis et al. showed a positive association between the size of the skin test response and the severity of latex-induced clinical allergic responses (25). Prick prick testing with several raw fruits and vegetables may give additional information in the diagnosis of latex-fruit syndrome.

The Latex Allergy Task Force of the EAACI is already working on solving these problems and should soon clarify the present confused situation.

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