

Latex and food allergy

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INTRODUCTION

Allergic reactions to foods in latex-allergic individuals and allergic reactions to latex in food-allergic individuals have received growing attention since they were first described about a decade ago. Clinical reports have described allergies to a large and growing number of fruits and vegetables from phylogenetically different sources in latex-allergic patients. The fact that, compared to the general population, a large proportion of patients sensitive to natural rubber latex (NRL) were found to be allergic to one or more foods suggested that many of these reactions could be the result of an immunologic cross-reaction. Based on recently published immunologic studies, we now know that this is often the case, and a few of the allergens and epitopes responsible for these clinically-interesting problems have been identified.

First, though, what do we mean by the term *cross-reaction*? In strictly immunologic terms, it means that a patient's IgE is capable of reacting with an allergen that did not elicit it, i.e., this IgE is cross-reactive [34]. In practice, however, the situation in NRL-allergic patients is not always so simple. Identification of the offending food substance sometimes requires much detective work. Moreover, in the clinic it is often impossible to know which substance, NRL or food, was res-

ponsible in the first place for inducing the cross-reacting antibody.

According to Vuitton [59], « cross-reaction » is an umbrella term for several different situations. First, the allergen that originally induced the IgE may be « hidden » (e.g., peanut proteins as an additive to other foods), or it may be present in a number of different substances, closely related or not, with complete molecular identity of the allergen(s). Second, the allergen(s) is common to taxonomically closely-related species (e.g., shrimp and lobster), in which case the molecular identity of the allergens is partial rather than complete. Third, there are allergens of taxonomically unrelated species (e.g., shrimp and mollusks), or even from different phyla (e.g., latex and banana), which contain a common epitope. In each of these cases, the allergen or an epitope on the allergen is « shared » with the allergen in the other substance. All three types of cross-reactions can cause clinically significant allergic symptoms, and at least the second and third types have been reported in connection with NRL. In addition, there is another type of cross-reactivity, one which can be detected serologically but which appears not to be biologically important [58]. A word about this later on.

For a general review of allergic cross-reactions, I refer you to the forthcoming issue of *Clinical Reviews in Allergy and Immunology*. The review

by François Lavaud on cross-reactions involving NRL [38]) in that same issue is particularly relevant for today's presentation, and I acknowledge Dr. Lavaud's permission to use that article as the major source for my presentation. Let me say that I do not intend to go into detail here about NRL allergens, as that subject will be discussed quite well by today's other speakers.

Nearly all of the suspected cross-reactions reported in association with latex allergy are due to allergens of plant origin. The few reports incriminating non-plant foods, such as milk [10] or fish [44, 60], are thought to be coincidental in atopic individuals. This is where the use of the term « cross-reaction » needs to be put to the test.

EPIDEMIOLOGIC ASPECTS OF LATEX-ASSOCIATED FOOD ALLERGIES

Estimates of the prevalence of IgE-mediated food allergy in the general population range from 0.1 to 7 %. It is clear that clinically-significant food allergies in latex-allergic patients are much more frequent than that. Of the 30 latex-allergic patients reported by Wrangsj[†] et al. in 1988 [60], 25 (83 %) reported food intolerance, and in the series reported by Moneret-Vautrin et al. in 1993 [45], one third of the latex sensitive patients had a food allergy. Based on a number of reports, it appears that about 50 % of NRL allergic patients have evidence of a concomitant food allergy, with extremes from 30 to 80 % [14, 32, 38, 41, 49]. The frequency differs according to the selection of patients, the clinical data obtained and the test methods employed. For example, in the study by Beezhold et al. [10], among 47 subjects with a positive skin test to NRL (of whom only 17 [36 %] reported an actual clinical reaction to latex), while 33 (70 %) reported an allergy to food. Fuchs et al. [27] reported that 15 of 56 patients (27 %) with clinical, skin test and RAST evidence of latex allergy had a food allergy based on history and RAST. As is often the case, a positive RAST for one or more common foods was found in some of those who were not clinically allergic to the corresponding food. At the Centre d'Allergie of the Hopital Rothschild, my colleague Dr. Mounedji [46] recently found that among 28 patients who were clinically allergic and skin test positive to latex, 21 (61 %) were skin test positive to one or more fresh foods, and 13 of these 21 patients (62 %) were clinically allergic to the food(s) to which they were skin test positive. The fact that there are discrepancies between skin and/or serological tests and the clinical manifestation(s) of allergic sensitization in these reports confirms the difficulty of establishing a clear picture of the prevalence of these cross-reactions.

FOODS THAT HAVE BEEN ASSOCIATED WITH LATEX ALLERGY

Pr. Leynadier and our colleagues at the Centre d'Allergie of the Hôpital Rothschild, who have seen more than 400 patients with latex allergy in the past 10 years, called attention to the occurrence of food allergy in latex sensitive patients in 1989 [40]. Four of their first five patients had a positive skin test to banana, avocado, passion fruit, pear, grapefruit, tomato, mushroom and/or bell pepper. Later, Pecquet et al. [49] reported that 34 % of their latex sensitive patients were sensitive to banana, 25 % to avocado and 20 % to kiwi fruit. More recently, Mounedji et al. [46] found that among the 21 mentioned above who were skin test positive to at least one fresh food, there were 18 who reacted to banana, 16 to chestnut, 14 to avocado and 13 to kiwi. Among the other foods that induced a positive skin test reaction in these patients were peach (12), tomato (11), mango (11), pineapple (8), celery (8), cantaloupe (6), apple (5) and papaya (4). Thirteen (62 %) of the patients with a positive skin test to at least one food had experienced clinical manifestations of food allergy, the foods reported most frequently being avocado, banana, chestnut and kiwi in these patients. Eighteen patients had a positive skin test to more than four different foods, and of these patients, 15 were also allergic to at least one pollen.

M'Raihi et al. [47] were the first to describe the occurrence of a systemic allergic reaction caused by **banana** in a latex allergic patient. Mäkinen-Kiljunen et al. [41] reported that 16 (52 %) out of a group of 31 latex allergic, latex RAST-positive patients had allergic symptoms induced by eating bananas, including some who had had systemic reactions. Banana skin prick tests were positive in 11 (35 %) of the 31 patients. The same proportions were found by Guilloux et al. [32], while Beezhold et al. [10] found a slightly lower frequency (38 %) of latex sensitive patients with a positive skin prick test to banana. In many other reports, sensitivity to banana, with or without clinical symptoms, is among the food allergies most frequently found to be associated with NRL allergy.

Lavaud et al. reported the occurrence of allergy to **avocado** in patients with allergy to latex and banana [37]. Blanco et al. [14] described allergy to avocado in 17 patients, 10 (59 %) of whom reported having had immediate allergic reactions to latex. In that report, a skin prick test with fresh avocado was positive in all 17 patients but the size of the reaction varied with the variety of avocado, the *strong* variety inducing larger reactions than the *hass* variety. So, as with apple allergy [13], the variety of the fruit and also its maturity and the conditions of culture seem to play a role. In the

series reported by Ahlroth et al. [2], 7 of 11 latex allergic patients were found to have a positive skin prick test to fresh avocado.

Kiwi fruit, the edible fruit of the Chinese gooseberry vine, first appeared in western markets only about two decades ago but was soon recognized as being allergenic and later on as being associated with latex allergy. Gaignon et al. [28] described the case of an 8-year old boy who experienced rhinoconjunctivitis and edema of the lips upon contact with latex objects and after eating kiwi fruit and bananas. Among 47 latex allergic patients, Beezhold et al. [10] found 8 with a positive skin prick test to kiwi fruit, one of whom had had a systemic reaction to the fruit. Blanco et al. [15] described four latex sensitive patients who also reacted to kiwi fruit, in addition to being allergic to avocado. A weak correlation between kiwi fruit and avocado sensitivities has also been reported in patients with pollen allergies [25]. It should be noted that the kiwi allergens cross-react with birch pollen-specific IgE antibodies [53].

Spanish authors were the first to describe allergy to **chestnuts** in latex allergic patients [5, 19, 54]. Symptoms have followed ingestion of raw chestnuts and sometimes even when the patient was peeling these nuts. It was not mentioned in these reports whether cooked chestnuts caused symptoms in their patients.

In addition, there are many publications containing reports of associations between concomitant sensitivity to latex and various other fruits and vegetables [7, 16-18, 20-23, 26, 30, 40, 43, 52, 60]. The list currently includes, in addition to those mentioned above, the following foods: **almond, apple, beets, bread fruit, buckwheat, celery, citrus fruits, fig, grapefruit, hazelnut, lettuce, peach, peanut, pear, a number of spices, spinach, strawberry, sweet pepper, tomato, walnut and watermelon**. Also reported are **condurango bark** and **passion fruit**, medicinal plant extracts of which are used as infusions [24, 35, 50]. The enzymes **papain** and **bromelain**, present in papaya and pineapple, respectively, have been shown to cross-react with latex-specific IgE [9, 50, 57].

PLANTS OTHER THAN FOODS THAT HAVE BEEN ASSOCIATED WITH LATEX ALLERGY

Serologic cross-reactivity has been reported between NRL allergens and allergens from **ragweed** and Kentucky blue **grass pollens** [6], with a high frequency of IgE antibodies that react with NRL in sera from ragweed sensitive patients [53]. Merrett et al. [42] found that the latex-reactive IgE, which was detected in 7 % of a large set of sera from English blood donors, would in most

cases also bind grass pollen allergens. Mounedji et al. [46] reported that among her 28 patients who were clinically allergic to latex, 17 (61 %) had a history of pollinosis and a positive skin prick test to at least one pollen extract. Fuchs et al. [27] recently reported that 25 of 56 patients with latex allergy had a positive ragweed RAST (11 with RAST class > 3) and 26 had a positive mugwort RAST (14 with RAST class > 3). Thirty-eight of the patients (73 %) were clinically allergic to an aeroallergen (grass pollen?), 38 had a positive timothy grass pollen RAST, 30 were positive for the major timothy allergen Bev v 1 and 11 were positive for Bev v 2. In contrast, Mäkinen-Kiljunen found no correlation between latex RAST and birch pollen RAST results in sera from 47 NRL allergic patients [41]. The possible significance of the serological cross-reactivity between NRL and pollen allergens will be considered below.

In only a limited number of reports is there information on the important question of the sequence of sensitization to latex and other food or other allergens in patients with multiple allergies. Lavaud et al. [37] described patients who were first sensitized to banana, then to chestnut and avocado and then, after repeated exposures, to latex. Blanco et al. [14] described latex allergy preceding allergy to avocado in four patients, the reverse in two patients, and concomitant development of the two allergies in four other patients. At least in the case of food allergies, it is evident that any sequence is possible. On the other hand, in the series of patients described by Mounedji et al. [46], pollinosis, present in 61 % of the 28 patients, had preceded the onset of latex allergy in most cases. Immunological evidence cited below suggests that latex allergy begins after cross-reacting allergies in some patients and before cross-reacting allergies in others. We suggest that the solution to this riddle will yield important insights into the control of the IgE response.

It is not very surprising that latex from the common house plant *Ficus benjamina*, the **weeping fig**, can induce immediate hypersensitivity reactions in latex allergic patients. Although *F. benjamina* is not phylogenetically close to *H. brasiliensis*, their latexes do have similar properties [8]. Bircher et al. [12] showed that the allergens of the weeping fig are present not only in its latex but also on the surface of its leaves, which implies that they can become airborne. While the prevalence of allergy to *F. benjamina* has not been determined, it appears nevertheless that most patients who are allergic to this plant are not at the same time allergic to *H. brasiliensis* latex. Thus, Bircher et al. reported that only one out of a series of 15 patients allergic to ficus allergens had a positive

skin prick test to NRL, and this patient did not experience symptoms upon contact with latex goods. Bessot et al. [11] reported, however, that the one patient in their series of 10 ficus-allergic patients who had a positive skin prick test to NRL also had allergic reactions on contact with rubber goods. Recently, Halsey and Williams [33] recently reported that IgE binding to **ficin**, a protease isolated from the ficus tree *F. glabrata* that is used in a variety of different industrial applications, was detected in sera from 20/44 latex-allergic patients. **Cannabis**, which like the weeping fig belongs to the Moraceae family of plants, appears to contain allergens that can cause an allergic reaction in NRL allergic patients [31].

IMMUNOLOGIC STUDIES OF CROSS-REACTIVITY BETWEEN LATEX AND ALLERGENS OF OTHER PLANT SOURCES

IgE antibodies to food are frequently detected in the serum of latex-allergic patients

Mäkinen-Kiljunen [41] found that 31 (66 %) of a series of 47 patients clinically allergic to latex had a positive latex RAST and 55 % of them had a positive banana RAST. Twenty five (81 %) of the latex RAST-positive patients were also banana RAST-positive, and the latex RAST results correlated significantly with those of the banana RAST ($p < 0.001$). Blanco et al. [14] reported that the avocado RAST had a sensitivity of 70 %, banana 29 % and chestnut only 11 %. The serum of some of their patients was shown to contain IgE antibodies that reacted with several allergens present in avocado extract and in fresh latex. Based on the additional evidence that some of the sera reacted only with avocado allergens and others only with latex allergens, they suggested that there are multiple epitopes in both substances, some that are shared and others that are specific to each substance [15].

DeCorres et al. [19] reported that the chestnut RAST had a sensitivity of 83 % but almost none for banana allergy. Many patients allergic to the weeping fig - although not clinically allergic to NRL - have latex-specific IgE detectable by RAST, 4 out of 20 in the series reported by Axelsson et al. [8], 5 out of 8 in the series reported by Bircher et al. [12] and 4 out of 10 in the series reported by Bessot et al. [11]. Kurup et al. [36] measured specific IgE to banana, potato and wheat in sera of latex sensitive patients (only one of whom was clinically allergic to food) and sera from a series of normal controls and they found no major differences in specific IgE titers between the latex allergic and the normal subjects. We suggest that the difference between these results and those of other

publications could be due to differences in methods, including the reliability of the clinical histories, the quality of the reagents used and/or to the test methods used, or to a combination of all of these factors.

Cross reactivity as demonstrated by serologic inhibition methods

Significant cross reactivity between NRL allergens and banana allergens in RAST inhibition studies was first reported by M'Raihi et al. [47], then by Ross et al. [55]. Lavaud et al. [37] reported that banana and avocado extracts could inhibit the reciprocal RAST nearly completely, while both of them were capable of partial inhibition of latex RAST. Blanco et al. [14] reported that latex inhibited the avocado RAST by up to 74 %, with a pool of sera from 17 patients allergic to avocado. In the chestnut RAST, maximum inhibition by latex was 44 %, and in the banana RAST it was 28 %. Ahlroth et al. [2] found that NRL inhibited binding to an avocado disk and that avocado extract inhibited binding to a latex disk, both in a dose dependent manner. Similar studies reported by Mäkinen-Kiljunen [41] revealed maximal inhibition of 60 % reciprocally between latex and banana. Rodriguez et al. [54] and DeCorres et al. [19] reported similar results with latex and chestnut, although in the latter report, chestnut extract did not inhibit the binding of latex to the latex disk. Lavaud et al. recently have shown by immunoblot inhibition that cross-reacting antigens are present in latex, banana and avocado extracts [38]. This observation was confirmed for latex and banana by Alenius et al. [3], with evidence of 14 IgE-binding banana allergens of different molecular sizes. They found evidence that these allergens bound IgE in sera from 10 out of 22 latex sensitive patients. Recently, the same group [44] showed that cross-reacting IgE-binding epitopes are shared by a 33 kD banana protein and the major latex allergen hevein, which is the chitin-binding domain of the latex protein prohevein and has structural homology to several chitin-binding plant proteins [48]. In addition, Alenius et al. [4] recently showed that sera from a number of NRL-allergic patients bind to avocado, wheat germ and/or Swedish turnip in immunoblotting, and that the major latex allergen hevein inhibits binding to wheat germ and avocado. The cross-reacting allergen, profilin, a cytoskeletal actin-binding protein which is found in all eukaryotic cells, is present in small amounts in latex extracts and perhaps accounts for cross-reactivity in a limited number of cases [56]. Fuchs et al. [27] recently demonstrated substantial inhibition in quantitative CAP assays of IgE binding to high molecular weight latex allergens (30 to 60 kD) on preincubation of sera from their latex-allergic patients

Table I. – Comparison between *Hevea* species and other plants that are a source of cross-reactivity but which have no apparent botanical relationship

<i>Dicotyledons</i>	<i>Order</i>	<i>Family</i>	<i>Genus</i>	<i>Species</i>	<i>Common name</i>
Rosidae	Euphorbiales	Euphorbiaceae	<i>Hevea</i>	<i>brasiliensis</i>	Natural rubber tree
Rosidae	Fabales	Papilionaceae (leguminosae)	<i>Arachis</i>	<i>hypogaea</i>	Peanut/ground nut
			<i>Phaseolus</i>	<i>vulgaris</i>	Kidney bean
Magnolidae	Laurales	Lauraceae	<i>Persea</i>	<i>gratissima</i>	Avocado
Hamamelidae	Fagales	Fagaceae	<i>Castanea</i>	<i>sativa</i>	Chestnut
Caryophyllidae	Urticales	Moraceae	<i>Ficus</i>	<i>benjamina</i>	Weeping fig
Dilleniidae	Dilleniales	Dilleniaceae	<i>Actinidia</i>	<i>sinensis</i>	Kiwifruit
Dilleniidae	Violales	Passifloraceae	<i>Passiflora</i>	<i>edulis</i>	passion fruit
		Caricaceae	<i>Carica</i>	<i>papaya</i>	Papaya
		Cucurbitaceae	<i>Cucumis</i>	<i>melo</i>	Melon (cantaloupe)
Asteridae	Gentianales	Asclepiadaceae	<i>Marsdenia</i>	<i>condurango</i>	Condurango bark
	Polemoniales	Solanaceae	<i>Solanum</i>	<i>tuberosum</i>	Potato
			<i>Lycopersicon</i>	<i>hypersicum</i>	Tomato
			<i>Nicotiana</i>	<i>tabacum</i>	Tobacco
	Asterales	Compositae	<i>Ambrosia</i>	<i>elator</i>	Ragweed
<i>Monocotyledons</i>					
Commelinidae	Poales	Graminaceae	<i>Poa</i>	<i>pratensis</i>	Blue grass
			<i>Triticum</i>	<i>sativum</i>	Wheat
			<i>Oryza</i>	<i>sativa</i>	Rice
	Bromeliales	Bromeliaceae	<i>Ananas</i>	<i>comosus</i>	Pinapple
	Zingiberales	Musaceae	<i>Musa</i>	<i>acuminata</i>	Banana

(from Lavaud et al., in press)

with ragweed, mugwort and timothy grass pollen extracts. Timothy extract almost completely inhibited IgE binding to latex whereas the reverse was not true. This high degree of cross-reactivity was seen preferentially in patients whose latex allergy was diagnosed accidentally compared to patients who were frequently exposed to latex products. This led Fuchs et al. to propose the existence of two types of individuals with latex allergy. One type might be sensitized preferentially against pollen and other plant substances and exhibit allergic symptoms to latex caused by cross-reactive IgE antibodies. The other type might be sensitized to latex originally and display a low degree of cross-reactivity to pollen allergens.

IDENTIFICATION OF SOME ALLERGENS THAT CROSS REACT WITH NATURAL RUBBER LATEX

Many proteins of similar structure and function, and in particular their antigenic epitopes, are known to be widely distributed in the plant kingdom, which explains why, even though the plants concerned belong to very distinct families (Table I), we find cross sensitivities and cross allergies between NRL and plant-derived foods with no apparent similarity. As described elsewhere in this symposium, a large number of allergenic polypeptides have been identified in NRL. Table II lists a few of those that have been shown to share epitopes with proteins from other plant sources.

Table II. – Proteins of natural rubber latex that cross-react with proteins from other plants

<i>NRL protein (molecular weight, kD)</i>	<i>Cross-reacting protein</i>
Rubber elongation factor (14.6)	papain
Profilin (15)	ragweed
Prohevein (20)	N-acetyl glucosamine (cereals, barley root)
	Win 1, win 2 (solanaceae)
	CBP 20 and PR4 (tobacco)
Hevein (4.5)	? (banana, 33 kD)
Hevamine (30)	lysozyme (fig, papaya, avocado)
? (36)	1,3 b glucosidases (tomato, kidney bean)
? (46 and 110)	patatin (solanaceae)

(from Lavaud et al., in press)

CARBOHYDRATE DETERMINANTS REACTIVE WITH IgE

N-linked carbohydrate groups of glycoproteins induce IgE, leading to cross-reactivity between several foods and grass pollen allergens [1]. These so-called cross-reactive carbohydrate determinants (CCDs) are also found in insect venoms and certain seafood (e.g., crustaceans and mollusks). Anti-CCD IgE is estimated to be present in 10 to 15 % of people sensitized to grass pollen. Patients with IgE cross-reactivity selectively based on CCD-specific IgE antibodies do not experience symptoms of food allergy, i.e., this IgE has poor biologic activity. It can however, cause positive RAST results without apparent clinical signifi-

cance. Fuchs et al. [27] investigated the effects of deglycosylation on IgE binding to latex allergens. Nitrocellulose-blotted latex extracts treated with periodate (a deglycosylating agent) and then incubated with cross-reactive sera revealed that the IgE-binding components of 30 to 60 kD present in latex contained epitopes that were sensitive to periodate treatment, suggesting that carbohydrates contribute to the binding of these epitopes. Specifically, the 60 kD latex allergen could be related to a previously-reported cross-reactive 60 kD mugwort glycoprotein allergen. To what extent such CCD determinants might be responsible for the cross-reactivity between latex and other plant-derived allergens remains to be determined. Fuchs et al. believe that latex-allergic patients whose IgE is strongly reactive with this high-molecular-weight glycoprotein allergen were probably initially sensitized against pollen. Prospective studies should be done to test this interesting hypothesis.

PRACTICAL CONSIDERATIONS

Faced with a patient claiming to be allergic to an NRL product, establish the diagnosis by taking a thorough history. Confirm the history by a skin prick test with a standardized latex allergen extract (e.g., Laboratoires Stallergènes) and a CAP RAST (Pharmacia). If in doubt, do a use test. Equally important, question the patient carefully about food allergies. In the *absence* of a positive or suggestive history of food allergy, we do not recommend routine skin prick testing with food extracts. First, the predictive value of such tests has not been established. Second, in most cases the results will not change our recommendations to the patient, since there is still no scientific basis for making a recommendation in this type of case. If the latex-allergic patient's history is *positive or strongly* suspicious of a food allergy or allergies, then skin prick testing should be done with the suspected food allergen(s). Since commercial extracts of the foods most commonly associated with NRL allergy are not yet standardized, we recommend prick testing through the fresh food when possible. Unfortunately, the predictive value of a skin test with the majority of food extracts has not been established. A CAP RAST may also be done to confirm the diagnosis, keeping in mind that the predictive value of many of the food RASTs has also not been established. If still in doubt about the food allergy, then one can do a double blind placebo controlled food challenge (the « gold standard »).

Since atopic individuals are at risk for NRL allergy, we routinely ask all patients who come for an allergy consultation about allergy to latex and, of course, about food allergies. It is certainly a good idea to inquire about food and NRL allergies before any medical, surgical, gynecological or

dental procedure that involves contact with a latex device, primarily latex gloves. In the case of patients who are at greater risk for NRL allergy, i.e., children who have had multiple surgical interventions and people who have frequent contact with latex goods in their occupation, it is especially important to inquire about the possibility of pre-existing food allergies, as this may give a clue to a possible NRL allergy.

Our recommendation for NRL-allergic/food-allergic patients is, of course, avoidance. When the NRL-allergic patient is not clinically food-allergic and has no positive skin prick test to foods, then we merely caution the patient to be aware of the possibility of future reactions to the most commonly implicated foods, i.e., banana, avocado, chestnuts and kiwifruit. When, as is frequently the case, the NRL-allergic patient is not clinically food-allergic but has a positive skin prick test to foods, then we are more cautious and we advise the patient to avoid eating the food(s) to which he/she has a positive skin test or RAST. We do this in spite of the fact that we do not know whether this advice is justified. And we try to see the patient at least once a year to see if a new food allergy has developed.

Finally, the efficacy and safety of specific immunotherapy for occupational asthma due to NRL allergy is currently undergoing a clinical trial at the Hôpital Rothschild and in several other allergy units in France. We expect that the results of this trial, sponsored by Laboratoires Stallergènes, will be known early this year. On the other hand, specific immunotherapy is not recommended for (most?) food allergies. It will be interesting to see what effect, if any, immunotherapy with NRL will have on concomitant food allergies.

CONCLUSION

Polypeptides with shared allergenic properties are present in NRL and wide variety of phylogenetically unrelated plants, particularly those consumed as food as well as some common pollens, providing an explanation for the numerous cross-reactions that have been reported. To date, however, only a few of the allergens responsible for these cross-reactions have been well characterized, and their clinical importance remains to be explored. We expect much progress will be made on this extremely interesting subject in the coming decade.

We are all exposed to food and to NRL from our earliest days. Why do some of us become allergic to one or more of these substances? That is the fundamental question that we must ask ourselves. The frequent concomitant occurrence NRL allergy and food allergy provides a valuable research opportunity that we should not miss.

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