

TABLE I. Characteristics of subjects infected with hMPV

Group	Number	Age	Sex	Serum IgE level (IU/mL)	Month of admission
Wheezing subjects	*1	2 mo	F	<2.0	Oct
	*2	2 mo	M	<2.0	Jan
	3	4 mo	M	<3.0	Jan
	4	8 mo	F	<2.0	Mar
	*5	9 mo	F	2.45	Feb
	6	12 mo	F	14.4	Mar
	7	13 mo	M	33.7	Jan
	8	5 y	F	27.6	Apr
	9	8 y	M	145	Apr
	10	9 y	M	548	Jan
				Mean, 128	
Control subjects	*11	6 mo	F	<2.0	Mar
	12	5 y	M	66.4	Feb
	13	9 y	F	1053	Oct
				Mean, 560	

*These subjects also tested positive for other viruses, including parainfluenza virus (subject 1); cytomegalovirus (subject 2); adenovirus, RSV, cytomegalovirus, and parainfluenza virus (subject 5); and rhinovirus and parainfluenza virus (subject 11).

children hospitalized for wheezing.⁷ In addition, the large majority (at least 80%) of the wheezing children age 3 years and older who were hospitalized in Virginia had striking atopic characteristics.¹

Combined with test results for other viral pathogens reported previously in the same patients,¹ the detection of hMPV in our current analysis increased the overall prevalence of viral infections among the wheezing subjects younger than 3 years to almost 90%. These results confirm and strengthen the observation that viral respiratory tract pathogens are the dominant risk factor for wheezing exacerbations in early childhood. Similar to other viruses that are significantly associated with wheezing during early childhood, more information is needed about the infants who are infected with hMPV and their long-term prognosis with respect to persistent wheezing and their risk for developing asthma.⁸

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Detection of novel latex allergens associated with clinically relevant allergy to plant-derived foods

To the Editor:

During the last decades, hypersensitivity to natural rubber latex proteins has become a serious occupational and public health problem. Several latex allergenic proteins have been purified and characterized thus far, and some of them have been shown to be responsible for the so-called latex-fruit syndrome caused by the presence of cross-reacting homologous proteins in fruits and vegetables.^{1,2} Banana, avocado, chestnut, and kiwi are the most frequently implicated foods in this syndrome, but associations with several other fruits and vegetables, including pineapple, fig, passion fruit, mango, tomato, bell pepper, carrot, oregano, dill, and sage, have been reported.

The allergen responsible for most cases of latex-fruit syndrome is hevein (Hev b 6.02), the amino-terminal fragment of prohevein³; homologous proteins have been detected in avocado, chestnut, banana, kiwi, tomato, passion fruit, papaya, and mango.³ Another latex allergen possibly causing food allergy is β -1,3-glucanase (Hev b 2), a 35-kd protein³; homologous proteins have been detected in avocado, chestnut, banana, kiwi, fig, and bell pepper.⁴ Finally, cross-reactivity between Hev b 7 and patatin has been recently described.⁵ In the present study we describe a patient who was sensitized uniquely to uncharacterized high-molecular-weight latex proteins cross-reacting with proteins in plant-derived foods.

A 53 year-old man was seen in September 2003 with a clinical history of eczematous dermatitis at the left foot for 12 years, at the left axilla for 1 year, and at the left ankle and both wrists for some months. Moreover, the

patient reported rhinoconjunctivitis after exposure to cat dander for some years. The man had undergone several surgical treatments in the past, including appendectomy at the age of 13 years; tonsillectomy at 21 years; phymosis at 30 years; cholecystectomy at 38 years; inguinal hernia at 39, 40, and 45 years; and dental surgery at 52 years.

Patch tests with a standard series of 20 substances recommended by the European Environmental and Contact Dermatitis Research Group (Hermal, Reinbeck, Germany) showed weak reactivity to paraben mixture. Skin prick tests (SPTs) with commercial extracts (Allergopharma, Reinbeck, Germany) of all main airborne allergens showed hypersensitivity to cat dander, grass pollen, and *Candida albicans*. The patient was considered to have cat allergy and atopic eczema. In August 2004, the patients asked for an urgent control visit. In June, 30 minutes after drinking a milkshake containing peach, banana, and grapefruit, he experienced severe dyspnea and pruritus at both hands. Symptoms lasted about 1 hour and gradually subsided. In July, there was a further episode of severe dyspnea and generalized urticaria-angioedema about 30 minutes after eating some fresh plums. This time he was immediately brought to the emergency department, where inhaled salbutamol, intravenous corticosteroids, and antihistamines were given.

Subsequently, the man noted itching and urticaria at his hands when he wore natural rubber latex gloves for gardening. An SPT with natural rubber latex extract (0.5 mg/mL; ALK-Abello, Hørsholm, Denmark); commercial extracts of egg white, cow's milk, shrimp, codfish, peanut, wheat, maize, green pea, soybean, tomato, carrot, orange, potato, peach, celery, almond, banana, melon, and hazelnut (ALK-Abello; 5% wt/vol); and purified apple lipid transfer protein (50 µg/mL; Institute of Food Research, Norwich, United Kingdom) showed hypersensitivity to natural rubber latex (wheal size, 8 × 8 mm) and potato (4 × 5 mm). All the remaining foods scored negatively. Further SPTs with fresh vegetable foods either involved in allergic reactions or known to be associated with latex allergy were positive for kiwi (wheal size, 15 mm × 8 mm), apricot (15 × 7 mm), plum (18 × 10 mm), peach (4 × 5 mm) raw potato (4 × 4 mm), apple (3 × 3 mm), tomato (6 × 4 mm), papaya (5 × 5 mm), mango (3 × 4 mm), and raw chestnut (3 × 3 mm); fresh banana and avocado did not elicit any skin reaction. SPTs with fresh boiled (100°C for 30 minutes) vegetable foods were performed to evaluate the heat stability of the allergens involved: tomato and chestnut elicited the same skin reactions as their raw counterparts, apple showed a marked reduction in skin reactivity (wheal size, 1 × 1 mm), and both boiled and oven-cooked potato did not elicit any skin reaction. Finally, SPTs with a commercial apricot jam, as well as both raw and boiled commercial dried plums, did not induce any skin reaction.

The patient reported the daily intake of both fresh tomatoes and apples without any problem. Thirty grams of boiled potato (100°C for 30 minutes) did not induce any adverse reaction on oral challenge. In view of the severity of the 2 recent episodes of food allergy, because of ethical

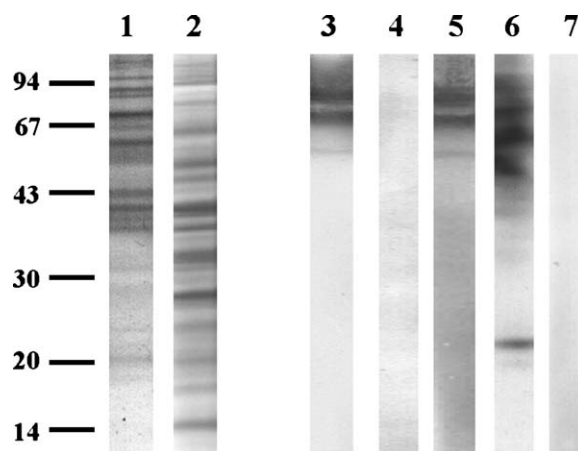


FIG 1. SDS-PAGE: lane 1, SDS-PAGE of plum extract; lane 2, SDS-PAGE of latex extract. Immunoblotting: lane 3, IgE reactivity of patient's serum to plum extract; lane 4, IgE reactivity of patient's serum to plum extract after incubation with natural rubber latex extract; lane 5, IgE reactivity of patient's serum to plum extract after incubation with house dust mite extract; lane 6, IgE reactivity to latex of patient's serum; lane 7, IgE reactivity to latex of a normal serum.

reasons, oral challenges with apricot, plum, peach, and kiwi were not carried out.

Natural rubber latex (B and C serum fraction,⁶ supplied by Prof Esah Yip, Rubber Research Institute of Malaysia) was centrifuged at 20,000 rpm at 4°C for 1 hour. Supernatant was gel filtered on a Sephadex G25 column (PD10; Pharmacia, Milan, Italy) and equilibrated with PBS containing 0.05% NaN₃. Fractions corresponding to the excluded peak were then collected and used for *in vitro* experiments. Plum, peach, kiwi, and potato purchased at a local supermarket were homogenized and used in immunoblot experiments carried out as previously described.⁷ Immunoblot experiments were carried out under both nonreducing and reducing conditions. In inhibition experiments 200 µL of either natural rubber latex (10 mg/mL) or house dust mite (4.8 mg/mL) were added to 800 µL of patient serum before immunoblotting was carried out.

SDS-PAGE and immunoblot analysis results are shown in Fig 1. The patient's serum showed an extremely strong IgE reactivity to natural rubber latex proteins in the 60- to 80-kD range and a much weaker reactivity at about 22 kD; no reactivity was observed at different molecular weights. No difference between immunoblots carried out under nonreducing or reducing conditions was observed. On immunoblotting with plum extract, the patient's serum showed IgE reactivity to a doublet at about 60 to 80 kD that was unaffected by preabsorption with house dust mite extract but was totally abolished by preabsorption with natural rubber latex. Immunoblot results with potato, kiwi, and peach were negative (not shown).

Allergy to Prunoideae (eg, plum, peach, apricot, and cherry) is rather infrequent in patients with latex allergy. In one large study less than 10% of patients with latex allergy reported clinical symptoms induced by peaches, and only

I had plum allergy.² This patient was not sensitized to lipid transfer protein, Bet v 1 homologue proteins, or profilin, and inhibition experiments demonstrated the immunologic cross-reactivity between latex and plum allergens. Interestingly, he was sensitized only to latex proteins the molecular weight of which exceeds that of all the proteins responsible for latex-fruit syndrome characterized thus far.⁸ One study⁹ reported hypersensitivity to cross-reacting proteins in latex and kiwi at 43 and 67 kD; our patient reacted uniquely to latex proteins in the 60- to 80-kD range. Although we were not able to detect IgE reactivity to vegetable foods other than plum in our *in vitro* experiments, the clinical history, as well as the SPT results, strongly suggest a possible cross-reactivity between the high-molecular-weight latex protein involved in this case and other plant-derived foods. Interestingly, heat-processed potatoes did not evoke any skin reaction and were tolerated on oral challenge, suggesting the heat lability of the allergen. Furthermore, the onset of systemic allergic reactions on ingestion of offending foods suggests that the responsible allergen is pepsin resistant. It is difficult to establish whether latex allergy preceded or followed food allergy in this patient; the fact that our patient underwent an unusually high number of surgical treatments in the past might suggest that latex was the primary sensitizer. The total inhibition of IgE reactivity to plum by latex seems to support this view. Our patient experienced his first reaction after the ingestion of banana (negative SPT result) and peach; on SPTs, peach induced a wheal-and-flare reaction similar to that induced by potato and tomato, both of which he tolerated. The heat lability of the allergen might explain potato tolerance, whereas cooking did not alter tomato reactivity on the SPT. One explanation might be that the ingestion of a whole peach as a milkshake caused a more rapid absorption of the offending allergen than eating a similar amount of solid fruit.

In conclusion, this study demonstrates that sensitization to high-molecular-weight latex allergens might cause cross-reactivity to Prunoideae and that such cross-reactivity might be clinically relevant.

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Importance of mixture of minor determinants and benzylpenicilloyl poly-L-lysine skin testing in the diagnosis of β -lactam allergy

To the Editor:

β -Lactams are the most common class of antibiotics inducing drug allergic reactions.¹ β -Lactams are low-molecular-weight molecules that function as haptens. These are capable of inducing immediate IgE-mediated and nonimmediate, mostly T cell-mediated allergic reactions. These reactions can be induced by all β -lactams, ranging from penicillin G (benzyl penicillin) to those newly introduced.² Thus not only the major penicillin determinant benzylpenicilloyl and some minor determinants are currently involved but also a few other conjugates.²

Skin tests represent the first step for the confirmation of an immediate allergic reaction to β -lactams. Guidelines for performing skin tests have been published by the European Network on Drug Allergy (ENDA), and they are used in most European centers dealing with drug allergy.^{2,3} It was proposed to use commercially available haptens to major and minor determinants (benzylpenicilloyl poly-L-lysine [PPL] and a mixture of minor determinants [MDM]), penicillin G, injectable amoxicillin, and ampicillin and cephalosporins if they are incriminated by the patients.⁴⁻⁶ However, both PPL and MDM commercialization has been stopped in most countries. In previous studies PPL and MDM skin tests were reported,² but there is no assessment of their importance using the ENDA recommendations.

In this retrospective analysis of the clinical case series of one drug allergy department, we evaluated the effect of such a withdrawal from the market for the diagnosis of β -lactam allergy.

Between September 1996 and August 2004, we included all the patients who had consulted at our allergy clinic (University Hospital of Montpellier, France) with a clinical history suggestive of a β -lactam allergy. We did not include patients with noncompatible clinical symptoms and signs, with symptoms disappearing without cessation of the suspected causal drug, and with reactions