

Allergy to white potato

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Allergy to potato is uncommon, and even more uncommon is allergy to potato pollen. The occurrence of both phenomena in the same patient made it possible to study cross-reactivity patterns of potato antigens. An 11-year-old girl, exclusively breast-fed for her first 4 months, developed anaphylactic symptoms after ingestion of potato at 5 months of age when she was fed potato for the first time. Subsequently, she developed urticaria, angioedema, and respiratory and systemic symptoms on contact with potatoes, ingestion of potatoes, and exposure to cooking potatoes or potato pollen. Three allergenic extracts from potato pulp, peel, and pollen were prepared. Polyacrylamide gel electrophoresis in the presence of sodium dodecyl sulfate and isoelectrofocusing of the three extracts were performed. IgE-mediated allergy to these extracts was demonstrated by means of immediate skin test reactivity, positive passive transfer, RAST, RAST inhibition, and leukocyte histamine release. Sodium dodecyl sulfate-polyacrylamide gel electrophoresis of the pulp extract followed by electroblotting and autoradiography demonstrated specific IgE antibodies directed against several proteins ranging from 14,000 to 40,000 daltons. (J ALLERGY CLIN IMMUNOL 78:1110-14, 1986.)

Potato is a common dietary constituent throughout the world, especially in Europe. However, there are few cases recorded in the literature of adverse reactions to potato. Pearson¹ described 29 female subjects with asthma who noted sneezing and/or wheezing while they were scraping uncooked potatoes. Nater and Zwartz² described a 24-year-old woman who suffered from allergic reactions after inhalation of finely dispersed particles of raw potatoes. Little is known about the allergenicity of both potato and potato pollen, and it is not known whether there is cross-reactivity between their allergens. We recently had the opportunity to observe an unusual case of IgE-mediated allergy to potato in which the allergens implicated were present not only in the whole potato but also in the potato pollen of the plant. We characterized the electrophoretic, biologic, and immunologic properties of the proteins present in potato pulp, peel, and pollen and investigated their cross-reactivity.

Case report

The subject was an 11-year-old girl, with no family history of allergy, exclusively breast-fed during her first 4

Abbreviations used

SDS-PAGE: Sodium dodecyl sulfate-polyacrylamide gel electrophoresis
P-K: Prausnitz-Küstner test
IEF: Isoelectrofocusing

months. At 4 months of age, corn and wheat flour were introduced in small amounts to her diet and were well tolerated. Initial contact with potato at 5 months (one teaspoonful of puree) was immediately followed by vomiting, erythema of the neck and face, and hypotension. Subsequently, skin contact with raw potato with or without the peel induced immediate localized urticaria and/or angioedema and conjunctivitis. Exposure to the odor of cooking potatoes provoked immediate conjunctival and pharyngeal itching and cough, followed by rhinorrhea, chemosis, sneezing, and wheezing if she remained in the vicinity. Symptoms disappeared spontaneously, rapidly, and without sequelae on cessation of the exposure. Ingestion of foods that contained potato as an additive (yogurt, cheese, cured meats, and pastry) provoked urticaria and angioedema of the face and lips, itching of the mouth and throat, cough, and sometimes sneezing and wheezing, depending on the potato content of the food. When she was in a rural area where potatoes were stored, she experienced pharyngeal pruritus, facial angioedema, and sometimes sneezing. Walking through a field of potatoes during pollen season provoked asthma that required treatment with bronchodilators. Otherwise, if the patient stayed away from potatoes, she was asymptomatic. Physical examination results and routine laboratory findings

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were normal. Sinus and chest x-ray films and spirometry were also normal.

MATERIALS AND METHODS

Antigen preparation

After separating pulp from peel, 5% extracts (weight per volume) of each were prepared in phosphate-buffered saline by stirring for 18 hours at 4° C. The procedure was identical for pollen collected from potato-plant flowers during the pollen season. The supernatants, after centrifugation (6000 × g for 30 minutes), were filtered (Millipore [Millipore Corp., Bedford, Mass.] and Wattmann, No. 20). Filtrates were dialyzed against 0.01 mol/L of glycine and were lyophilized. The total protein in each of the three lyophilized extracts was determined by the Lowry method with a bovine-albumin standard.

Electrophoresis of potato pulp, peel, and pollen extracts

SDS-PAGE was performed according to the original method described by Laemmli³ and modified by Hudson and Hay⁴ with the three extracts at 2 mg/ml of protein concentration. IEF in polyacrylamide gels (LKB, Uppsala, Sweden) was performed according to the manufacturers instructions with minor modifications⁵ at a pH range of 3.5 to 9.5, and extract protein concentration of 2 mg/ml.

In vivo testing

Prick skin tests were performed with pulp, peel, and pollen extracts at 1 mg/ml concentration on the patient and several healthy control subjects. The patient was also tested with 25 commercially available common inhalant extracts, including 14 pollens of trees, weeds, and grasses, and eight different molds, mite, and dust. Food allergens included bovine-milk proteins, egg proteins, several species of fish, and tomato. Histamine dihydrochloride, 0.1%, was used as a positive control, and 50% glycerol was used as a negative control. All skin test sites were read after 15 minutes, and a wheal of at least 3 mm by 3 mm was considered as positive. A passive transfer test (P-K) with the patient's undiluted serum, previously screened for Australian antigen, was performed on a healthy nonallergic volunteer (patient's mother). Fresh patient-serum samples of 0.1 ml were injected intradermally into the recipient's right forearm, and 0.1 ml of serum previously heated at 56° C for 4 hours was injected in the left forearm. The passive transfer sites on both forearms were challenged after 48 hours with 0.05 ml of each extract. After the P-K testing was completed, the mother was asked to ingest potato to demonstrate the reaction first described by Walzer¹⁶ in 1927 that bears his name.

In vitro testing for total and specific serum IgE

Total serum IgE concentration was determined by the PRIST (Pharmacia Diagnostics, Uppsala, Sweden). Potato pulp, peel, and pollen allergens in solution were coupled to CNBr-bromide-activated filter paper discs with 200 µl of

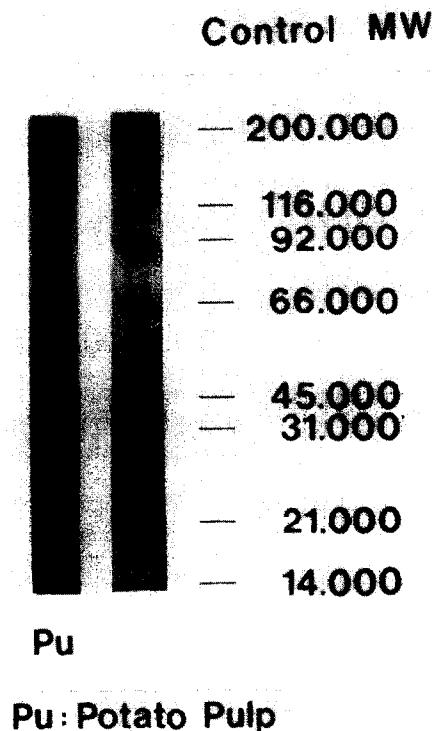


FIG. 1. Electrophoresis of pulp extract in polyacrylamide 8% gel containing SDS; 50 µg of pulp extract protein equivalent was loaded into the gel.

solution per disc, according to the method of Ceska and Lundkvist.⁶ The quantity of specific IgE bound to a disc is expressed as a RAST score as suggested by the manufacturer (Phadezym RAST, Pharmacia AB, Uppsala, Sweden). We have defined a RAST score of 2 and higher as positive. Proteins separated by SDS-PAGE of pulp extract were transferred electrophoretically to a nitrocellulose membrane. IgE-binding zones on the membrane were identified by the application of patient serum and ¹²⁵I-labeled rabbit antihuman IgE (Pharmacia) according to the original electroblotting method of Erlich et al.⁷ modified by Sutton et al.⁸ A second nitrocellulose membrane with the same proteins transferred was incubated with sera from a dust-sensitive atopic individual with high specific IgE levels to dust.

RAST inhibition

Samples of patient serum were incubated with pulp and pollen extracts at tenfold increasing concentrations from 0.001 mg/ml to 10 mg/ml. After 18 hours of incubation, pulp and pollen discs were added, respectively, and RAST was performed as described above. Crossed RAST inhibition was achieved by adding pulp discs to samples of serum incubated with pollen extract and pollen discs to samples of serum incubated with pulp extract. The capacity of each extract to inhibit binding of specific IgE to the related and unrelated disc was expressed as a percentage of 100% (total inhibition (RAST score of 0)).⁹

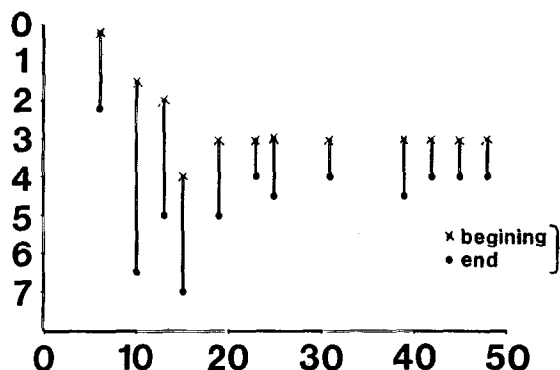


FIG. 2. Walzer reaction. The x axis represents the lapse of time from the injection of serum (P-K) in days. P-K was performed in day 0. The y axis represents the period of time between ingestion of potato-containing food and reaction in recipient in hours. The P-K recipient scheduled every local reaction appearing after ingestion of foods containing known or unknown amounts of potato; x represents the beginning and • the end of the reaction. The bars illustrate the total duration of the reaction.

Histamine release

Whole blood samples from the patient were incubated with serial tenfold concentrations of pulp and pollen extract, respectively, from 1 ng to 100 $\mu\text{g/ml}$. Histamine release from the patient's leukocytes after allergen challenge was determined with an enzymatic isotopic microassay with s-adenosyl-L (methyl³H)-methionine (Radiochemical Center, Amersham, England) as methyl donor, and rat kidney as source of histamine-methyltransferase according to the slightly modified method of Taylor et al.¹⁰ The capacity of each extract to release histamine was expressed as a percentage of the total leukocyte histamine in the serum sample.

Non-IgE antibodies

An immunoenzymatic assay with a microtiter plate as solid phase (ELISA) was used to detect the presence of non-IgE antibodies in the patient's serum against potato pulp, peel, or pollen antigens.

RESULTS

Potato extracts

The protein content in each extract was 33 mg/ml. IEF of pulp extract demonstrated multiple bands ranging from pH 3.5 to 9.5. In peel extract the pattern was similar but with fewer bands and not as well defined. In pollen extract less protein bands were detected, particularly in the alkaline pH range. SDS-PAGE demonstrated that pulp extract contained numerous proteins, most at <40,000 daltons (Fig. 1). The peel pattern was similar to that of the pulp, and the pollen pattern demonstrated two slightly stained bands corresponding to proteins of 65,000 and 21,000 daltons.

Patient sensitization

The patient had positive skin tests to all three potato extracts and negative reactions to all the other pollens, molds, mite, and food extracts. The normal subjects had negative skin tests to all of these extracts. The P-K test was strongly positive with the three extracts in the right forearm (unheated serum) of the recipient and was negative in the left forearm (serum heated to 56° C). On ingestion of potato by the recipient, 24 hours after completion of the P-K, a wheal and erythema reaction accompanied by itching developed at all the unheated serum test sites. Subsequently, when the recipient ingested potato-containing food (yogurt, cheese, cured meats, and pastry), similar reactions were noted at the test sites. Some of the reactions persisted for up to 5 hours (Fig. 2). Initially, the test sites flared at 10 minutes after potato-containing food was ingested. During the next 7 weeks, the reactions appeared later, were less intense, and did not persist as long. By day 60, the test sites no longer reacted to the ingestion of potato-containing food. However, at this time, challenge of the P-K sites with potato extracts demonstrated a positive reaction with wheal, erythema, and itching. The recipient claimed that even 6 months after the passive transfer, potato ingestion resulted in itching at the injection sites. The patient's serum exhibited a significant degree of potato-specific IgE antibodies, as evidenced by a RAST class 4 for pulp and class 2 for pollen. RAST for peel extract was not performed. Histamine release from peripheral blood basophils with pollen and pulp extracts demonstrated that 50% histamine release was achieved by previously incubating a serum sample with pollen extract at 1 $\mu\text{g/ml}$ or with pulp extract at 10 $\mu\text{g/ml}$. There were no significant amounts of non-IgE antibodies against pulp, peel, or pollen extracts by ELISA. Total serum IgE was 800 kU/L.

RAST inhibition

RAST inhibition with pulp and pollen extracts demonstrated a good dose-response relationship. RAST with pollen discs was 50% inhibited, previously incubating the serum samples with pollen extract at 60 $\mu\text{g/ml}$. RAST with pulp discs was 50% inhibited by previously incubating the sample with pulp extracts at 70 $\mu\text{g/ml}$. Crossed RAST inhibition demonstrated the pulp extract at any concentration, ranging from 0.01 to 10 mg/ml, inhibited RAST with pollen discs by 82% to 98%. Pollen extract at any concentration from 0.01 to 10 mg/ml demonstrated no detectable inhibition of RAST with pulp discs.

IgE-specific binding

Autoradiography of the electroblott of pulp extract demonstrated IgE binding to major stained proteins

detected after SDS-PAGE (Fig. 3). Specific binding of IgE from the potato-allergic subject for these proteins was substantiated by finding absence of binding of serum IgE from a dust-sensitive atopic individual to these potato proteins.

DISCUSSION

Food allergens are known to be mostly glycoproteins ranging from 18,000 to 36,000 daltons. These allergenic proteins represent only a small proportion of the total protein content of food.¹¹ Potato is rarely known to cause food allergy. Its biochemical composition includes proteins, glycoproteins, and alkaloids (including solanine). Potato-related vegetables that belong to the solanaceae family include cherry ground, eggplant, melon, pear, paprika, peppers, bell, cayenne pepper, red pepper, tobacco, tomato, strawberry tomato, and chili.¹¹ Anaphylaxis has been documented after ingestion of potatoes,¹¹ and asthma has been reported when new potatoes are peeled.¹² In addition, some patients who are allergic to birch-tree pollen may suffer allergic reactions to potatoes.¹²

In the present study the analysis of three potato extracts by SDS-PAGE and IEF demonstrated that the peel extract was similar to the pulp, indicating that most of the proteins of peel extract were also in pulp. However, it is technically difficult to separate peel from pulp, and some contamination of peel with pulp may have occurred. Pollen extracts demonstrated few bands by IEF and SDS-PAGE. Nonetheless, allergenicity of the pollen was demonstrated by means of *in vivo* and *in vitro* tests. Pulp and pollen extracts were antigenically related, as demonstrated by the fact that pulp was able to completely inhibit RAST to pollen. However, RAST with pulp discs could not be inhibited by incubation with pollen extract. This demonstrated that all allergenic determinants in potato pollen were present in pulp, but the dominant pulp-specific determinants were not present in pollen. The chemical nature of the determinants causing cross-reactivity between potato pulp and pollen extracts have not been defined. The allergenic activity of pulp extract was not limited to a single, discrete protein. At least three proteins separated by SDS-PAGE demonstrated IgE binding.

The patient's IgE-mediated allergy to potato was demonstrated by means of skin testing RAST, histamine release, and passive transfer (P-K and Walzer reaction). Our patient's sensitivity had three important characteristics. First, a high degree of specificity was demonstrated by the fact that she reacted only against allergenic determinants present in potato pulp, peel, and pollen. She was able to eat all vegetables related to potato and could tolerate inhalation of other pollen than potato without symptoms. Second, a high degree

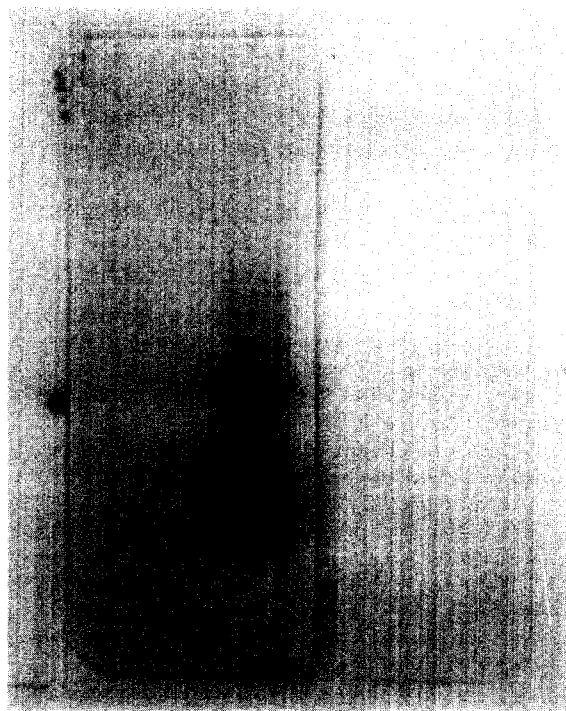


FIG. 3. Autoradiography of electroblotting analysis of pulp extract. Potato-pulp proteins separated by SDS-PAGE and transferred to a nitrocellulose membrane were incubated with patient serum (1/100 dilution) and then with ¹²⁵I-labeled antihuman IgE. For specificity control, a second nitrocellulose membrane with the same pulp-extract proteins that were transferred was incubated with serum from a dust-sensitive patient (1/100 dilution) with high specific IgE levels to dust and then with ¹²⁵I-labeled antihuman IgE demonstrating no binding to any transferred protein.

of IgE sensitivity was demonstrated by the fact that minute amounts of potato (even cooked) were able to elicit strong reactions in both the patient and the P-K recipient. In the previous reported cases of potato sensitization,^{1, 2} the patients tolerated cooked potatoes. Third, the long life of the transferred IgE exceeds all previous studies. Finally, this case again raises the important question of the mechanism of sensitization in early life. Sensitization without prior known exposure to a substance is widely described in literature.¹³ Sensitization is believed to occur either prenatally or in the postnatal period caused by inadvertent ingestion of food antigens in the diet or, in the case of exclusively breast-fed infants, to food antigens in breast milk.¹⁴ The presence of food antigens in breast milk was first described in 1930¹⁵ and has been reconfirmed in recent studies.^{13, 14} Some authors have suggested that this way of sensitization to food allergens could be the most important in infants.^{16, 17} Another possibility is transplacental antigen passage with intrauterine sensitization, documented by some au-

thors.¹⁸ Our patient could have been sensitized either by breast milk or within the uterus.

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