

Food skin testing in patients with idiopathic anaphylaxis

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Avoidance is the key treatment of anaphylaxis if an allergen exists; thus, we have evaluated 102 patients with the initial diagnosis of idiopathic anaphylaxis with a battery of 79 food-antigen skin prick tests selected to include foods reported or suspected of provoking anaphylaxis. Only those patients whose episodes consisted of at least two of the following were included in the study: angioedema with or without hives, laryngeal edema leading to severe dyspnea, hypotension, or loss of consciousness. Detailed history, physical examination, and conventional laboratory tests ruled out known causes of anaphylaxis. Thirty-two patients (31%) had positive tests to one or more food antigens. In five of these patients, subsequently eating a food that elicited a positive test provoked an anaphylactic reaction. Two patients eliminated the foods completely, stopped having reactions, and refused challenge. In these seven patients, 10 different antigens provoked anaphylaxis: aniseed, cashew nut, celery, flaxseed, hops, mustard, mushroom, shrimp, sunflower, and walnut. We conclude that a battery of selected food-antigen skin prick tests provided a useful method for identifying an offending antigen in these patients and that some (7% in our series) cases of "idiopathic" anaphylaxis by history are not truly idiopathic. (J ALLERGY CLIN IMMUNOL 77:516-19, 1986.)

Anaphylaxis, a systemic, life-threatening reaction, usually occurs because of hypersensitivity to foods, insect stings, drugs, or after exercise. The term "idiopathic anaphylaxis" refers to that group of patients with anaphylaxis of unknown cause. There have been several articles written recently concerning the idiopathic anaphylaxis syndrome and outlining appropriate methods to uncover known causes, especially food and drug ingestion.¹⁻⁵ Sonin et al.⁶ evaluated a group of 50 patients with idiopathic anaphylaxis, and all of these patients had no apparent food sensitivities. If the food history was completely negative, no food skin testing was performed. If there were any suspected food antigens in the history, then only these foods were skin tested. Some (21) of the 50 patients were skin tested for certain foods, and all tests were negative. Recently, several authors have reported unusual food antigens causing anaphylaxis,⁷⁻¹¹ the major reason for our interest in evaluating a group of such antigens in patients with idiopathic anaphylaxis.

We hypothesized that many uncommon food antigens may be ingested unknowingly in complex dishes like pizzas, salads, sauces, and certain ethnic foods. To test this hypothesis we performed skin prick tests with a battery of 79 food antigens in 102 patients with a diagnosis of idiopathic anaphylaxis. Seven subjects were identified whose anaphylaxis was apparently caused by an uncommon food. Our results would support the conclusion that food history and food diaries alone are not sufficient to identify all possible food-antigen sources capable of initiating a severe systemic anaphylactic reaction and that skin testing is a useful adjunct.

MATERIAL AND METHODS

One hundred sixty-eight patients observed at the Mayo Clinic between 1980 and 1984 received a battery of 79 skin prick tests to help evaluate and identify an antigen source responsible for systemic anaphylactic reactions (Table I). Of these 168 patients, only 102 had symptoms severe enough to be included in the present study. Five patients were found to have sensitivities to various dyes and preservatives, including one patient with sodium metabisulfite sensitivity. These patients were not included in the study. Symptoms necessary for inclusion in the study were two or more of the following: angioedema with or without hives, laryngeal edema leading to severe dyspnea, hypotension, or loss of consciousness. Detailed history and physical examination by a member of the Section of Allergic Diseases and Internal

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TABLE I.

Total No. of positive skin prick tests	Antigens*
0	Allspice
2	Almond
5	Aniseed†
0	Apple
1	Artichoke
1	Baker's yeast
0	Banana
0	Bay leaf
1	Beet
0	Black pepper
1	Brazil nut
2	Brewer's yeast
0	Buckwheat
0	Cantaloupe‡
1	Caraway seed‡
2	Cashew nut†
5	Castor bean
4	Celery†
8	Chamomile§
2	Chestnut‡
0	Chicken
1	Chicory
0	Chili pepper
0	Chocolate
0	Cinnamon
1	Clam
0	Clove
2	Coconut
0	Cod
0	Corn
1	Cottonseed
2	Crab
0	Cumin seed§
0	Dill seed
0	Egg
1	Fennel§
4	Filbert
1	Flaxseed
1	Garbanzo bean§
0	Garlic

*All antigens manufactured by Hollister-Stier Laboratories, Spokane, Wash., unless otherwise noted.

†Positive clinical correlation with skin test and anaphylaxis.

‡Manufactured by Allergy Laboratories of Ohio, Inc., Columbus, Ohio.

§Prepared in our research laboratory.

Medicine and pertinent laboratory data ruled out any known food sensitivities or other causes for anaphylaxis. Patients ranged in age from 10 to 73 years, with an average of 40.2 years. There was an approximately equal number of male and female subjects. If a particular food antigen was sus-

TABLE I. Cont'd

Total No. of positive skin prick tests	Antigens*
2	Ginger
1	Halibut
1	Honey
2	Hops†
3	Horseradish
0	Juniper berry
1	Lentil
1	Lima beans
2	Lobster
2	Mango
1	Milk
5	Millet§
3	Mushroom†
3	Mustard†
1	Nutmeg
0	Orange
0	Oyster
2	Pea
0	Peach
0	Peanut
1	Pistachio‡
3	Poppy seed
0	Potato
0	Psyllium seed
0	Raspberry
0	Sage
0	Salmon
2	Sesame seed
3	Shrimp†
0	Soybean
0	Strawberry
3	Sunflower†
0	Sweet potato
0	Tangerine
0	Tapioca
1	Thyme
1	Tumeric
0	Vanilla
1	Walnut†

pected by the patient or physician and the skin prick test was positive to this antigen, the patient was not included in the study, since this would not be considered a case of idiopathic anaphylaxis. However, if the patient or physician suspected food antigens in general as being a possible antigen source but without a clue to any specific antigen according to the patient's history or food diary, then the patient was included in the study.

The antigens were chosen to include those that have been reported to cause anaphylaxis as well as other spices or condiments, especially seeds. They were purchased from commercial sources when they were available. Chamomile,

TABLE II. The 10 antigens with positive clinical correlation

Antigens	Total No. of positive skin tests with positive correlation	Total No. of positive skin tests	Percent of positive skin tests with positive correlation
Aniseed	1	5	20
Cashew nut	1	2	50
Celery	2	4	50
Flaxseed	1	1	100
Hops	1	2	50
Mushroom	1	3	33
Mustard	2	3	66
Shrimp	1	3	33
Sunflower seed	1	3	33
Walnut	1	1	100

cumin seed, fennel, garbanzo bean, and millet were prepared in our research laboratory.

Skin prick testing was performed with a 1/20 w/v extract in 50% glycerine. The reaction was recorded as positive if the wheal was ≥ 5 by 5 mm, and a flare developed. Appropriate positive (histamine) and negative controls were placed.

Some patients were challenged after a positive food skin test at our institution, whereas most were either challenged by their local physician or later ate a food that had elicited a positive skin test. All patients either returned for follow-up evaluation or the follow-up evaluation was conducted by telephone with the patient or the local physician. We considered a challenge positive if the patient developed a severe systemic reaction equal to that necessary for inclusion in the study within 4 hours after ingestion of a food antigen that was skin prick tested positive. In addition, two patients were considered as having positive clinical correlation because elimination of a skin test positive food was followed by complete elimination of anaphylaxis for longer than 24 months. Patients with a positive skin test, but who had not been challenged, were designated as a negative clinical correlation. None of the 102 patients were receiving maintenance medications; all were treated acutely with antihistamines and/or adrenalin.

RESULTS

There was a total of 94 positive skin tests (Table I) with 12 tests in seven patients correlating positively to a clinical sensitivity (Table II). Thirty-two patients (31%) had one or more positive skin tests; seven (7% of the 102 patients) had a positive clinical correlation. Details of the seven patients with positive clinical correlation to a positive skin test are listed in Table III. All reactions to food antigens occurred within 4 hours of ingestion.

DISCUSSION

Patients with idiopathic anaphylaxis have no known allergic cause, and current literature supports the use of a detailed food history and recording of a food diary in the evaluation of these patients. Food skin testing is suggested only when the clinician's suspicion has been aroused by the history or food diary, and then only to proceed with testing of fairly major food groups.^{6, 12} Had we tested for only the suggested food antigens, we would have identified the causal agent(s) in patients Nos. 6 and 2, and one of the three antigens in patient No. 5. Six antigens (aniseed, flaxseed, hops, mustard, celery, and mushroom) and four patients would still have remained in the idiopathic anaphylaxis group, and patient No. 5 would continue to have anaphylaxis to two of the three antigens that would have remained unidentified.

An interesting finding in our study is the significantly lower age group of the patients with positive clinical correlation to a positive skin test. The average age of the positive correlation group was 27.7 years; whereas the average age of the entire group of 102 patients studied was 40.8 years. This may indicate that one should be more aggressive in skin testing younger individuals in search of an obscure food antigen.

Ideally, all 32 patients with a positive skin prick test to an antigen should have received a double-blind food challenge to those antigens. Unfortunately, this was not possible for a variety of reasons. RAST testing was not done to these antigens because most are not commercially available as RAST reagents. Also, it has recently been demonstrated that the addition of RAST testing added nothing to the diagnostic accuracy of the skin tests alone in the evaluation of children with atopic dermatitis and food hypersensitivity¹³ and that the sensitivity of the food skin prick test was equal to that of double-blind oral food challenge in identifying a causative agent.

No patient skin tested and demonstrated to have a positive clinical correlation to an antigen has had another episode of anaphylaxis during the 18 to 60 months since eliminating the antigen from their diet. The 25 patients with no clinical correlation to the positive skin prick test have not fared as well. Even on elimination of all positive skin test antigens, 21 of the 25 patients (82%) continued to have episodes of anaphylaxis 1 to 5 years later. Subsequent ingestion of skin test positive food antigens did not provoke anaphylactic reactions or increase the rate of attacks in these patients. However, none has died. It is not clear why some of these skin test positive antigens provoked anaphylaxis and others did not.

TABLE III. Details of the seven patients with positive clinical correlation to a skin prick test antigen

Patient No.	Age	M/F	Challenge and skin test positive antigens	No. of reactions after antigen elimination	Occurrence of other positive skin tests without positive correlation
1	26	M	Aniseed	None	Yes
2	24	M	Shrimp	None	No
3	43	F	Mustard, flaxseed	None	Yes
4	23	F	Celery, hops	None	Yes
5	34	F	Celergy, mustard, sun-flower	None	Yes
6	13	M	Walnut, cashew nut	None	Yes
7	31	F	Mushroom	None	No

In summary, a group of 79 uncommon food-antigen skin prick tests have identified a food antigen responsible for anaphylaxis in seven patients from a group of 102 patients with the initial diagnosis of idiopathic anaphylaxis. We recommend that at least the 10 different antigens with positive clinical correlation should be used in the evaluation of all patients with idiopathic anaphylaxis, regardless of the history. The remaining 69 antigens did not identify a causative agent in our group of 102 patients, but there have been case reports of many of these antigens causing anaphylaxis in some individuals. Thus, we recommend the use of a battery of uncommon food antigen skin tests in the evaluation of individuals with idiopathic anaphylaxis.

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