
Food allergy in human immunodeficiency virus (HIV) infection

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Background: Gastrointestinal complaints and pruritic skin conditions are common in patients infected with human immunodeficiency virus (HIV). Because atopic disorders such as drug allergy, asthma, and allergic rhinitis are apparently increased, we hypothesized that food allergy may also be more common in patients with HIV.

Objective: The purpose of this study was to estimate the prevalence of food allergy in patients infected with HIV.

Methods: Consecutive patients visiting our outpatient adult HIV clinic were screened for possible food allergy by use of a questionnaire. One hundred seventy-six patients responded. Sixty-two of these patients reported symptoms compatible with a possible food allergy. Followup of the 62 subjects was possible in 40. Thirty-one patients were skin tested for foods thought to produce reactions.

Results: Three patients (1.7%) described previous anaphylactic responses to specific foods and were therefore not skin tested or challenged orally. Six patients (3.4%) described very strong histories of food allergy but either refused or were too ill for testing. Twenty-nine of the 31 patients had negative skin tests. One of the two patients with a positive skin test to a suspected food also had a positive double-blind, placebo-controlled food challenge (DBPCFC). There was no correlation between CD4 cell count and likelihood of food allergy. Based on a strong history alone, the maximal estimated prevalence of food allergy in this group was 5.7% (10 of 176). By using the more strict criterion of positive DBPCFC, the prevalence of food allergy in this patient population was 0.57% (1 of 176).

Conclusion: These results suggest that food allergy is an uncommon disease in patients with HIV infection with an estimated prevalence similar to that found in the general adult population. Our data do not suggest an obvious direct correlation between HIV infection and food allergy.

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INTRODUCTION

Many authors have suggested that allergic disorders are more common in people with various immunodeficiencies^{1–12} including patients infected with human immunodeficiency virus (HIV).^{13–25} The majority of studies of the relationship between HIV infection and atopy have focused on adverse drug reactions and eczema-like skin disorders, but rhinitis and asthma have also been reported to occur more frequently in HIV-infected persons.²³ Immune system abnormalities including

an elevation in IgE are thought to play a major role in this allergic diathesis especially in the later stages of HIV infection.^{26,27}

Studies have also shown that children with immunodeficiency have a higher prevalence of food allergy compared with age matched controls,^{1–6,9,11,12} but data in adults with immunodeficiency disorders are limited. Since patients with HIV infection are often afflicted with symptoms reminiscent of food allergy, including gastrointestinal complaints and skin disorders, and because of the apparent increased frequency of several allergic disorders in people infected with HIV, we hypothesized that food allergy may also be more common. The purpose of this study was to estimate the preva-

lence of food allergy in adult patients infected with HIV.

METHODS

Men and women in our outpatient human immunodeficiency virus (HIV) clinic were evaluated for this study. The Institutional Review Board at Harbor-UCLA Medical Center approved the study, and written informed consent was obtained from each participating patient.

Consecutive patients visiting our adult HIV clinic from January to August of 1995 were asked to fill out a questionnaire related to symptoms of food allergy. An attempt was made to contact all patients who reported any of the following symptoms within four hours of eating: nausea or vomiting; diarrhea; abdominal pain or cramping; itching or swelling of the lips, mouth, tongue or throat; wheezing or breathing difficulty; itchy skin rash; itchy or watery eyes; itchy or runny nose. Subjects with reported severe systemic or anaphylactic reactions to specific foods (including angioedema, severe bronchospasm, or hypotension) were considered “positive” for food allergy and not skin tested or challenged orally. All patients contacted who reported a possible food allergy were included for further study. Patients whose symptoms were solely related to intolerance to lactose, “greasy,” “fatty,” or “spicy” foods were excluded. Other exclusion criteria included a known gastrointestinal infection, a known skin infection, “gustatory” rhinitis, or symptom onset correlating with a new medication.

Eligible patients were then skin tested by using a “multi-test” device with a panel of common food antigens including the following: milk, wheat, egg white, peanut, pork, corn, orange, tomato, celery, shrimp, soybean, broc-

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coli, and codfish. Additionally, patients reporting reactions to other specific foods were tested for those foods. A positive skin prick test was defined as a wheal greater than 2 mm in diameter (after subtracting the diameter of any wheal produced by a diluent control). Subjects with extensive skin disease or poor skin test response to a histamine control (wheal less than or equal to the diluent control) were tested by radioallergosorbent tests (RAST). Patients with positive skin tests or RAST were then tested by use of a double-blinded, placebo-controlled food challenge (DBPCFC) to confirm the diagnosis. All challenges were performed under closely monitored conditions with appropriate resuscitation equipment and medication available.

Descriptive statistical analysis was used to assess the prevalence of both probable and confirmed food allergy.

RESULTS

One hundred seventy-six patients (157 males and 19 females) responded to the questionnaire (approximately 40% of our total outpatient service). The CD4 cell count of this patient population consisted of the following: 0 to 200 (127 patients), 201 to 500 (34 patients), greater than 500 (14 patients), and one unknown. Of those who responded, sixty-two subjects were considered to have a possible food allergy. Follow-up of the 62 subjects was possible in 40 (22 could not be contacted, had moved, or died). Thirty-one subjects were skin "prick" tested. Three patients (1.7%) described previous anaphylactic responses to specific foods (one to mango, two to shellfish) and were therefore not skin tested or challenged orally. Six patients (3.4%) described very strong histories of food allergy (recurring reactions to specific foods commonly associated with food allergy) but either refused or were too ill for testing (Table 1). Twenty-nine of the 31 patients had negative skin tests, including five patients who gave strong histories for food allergy. One patient who had a poor histamine re-

sponse on skin testing was tested by RAST which was also negative.

Two patients had positive skin tests to suspected foods. One patient described nausea, abdominal pain, and headache within 30 minutes after eating broccoli. These symptoms recurred during DBPCFC. The second patient described "hives" within 20 minutes after eating red grapes. Skin testing to the peel and pulp of the red grapes was initially positive with an 8 mm wheal. After a negative DBPCFC to the same grapes, a repeat skin test to both peel and pulp was equal to control.

The estimated maximal prevalence of food allergy based on a strong history alone (without a negative skin test or negative DBPCFC) in our patient population was 5.7% (10 of 176). By using the more strict criterion of a positive DBPCFC, the prevalence of food allergy in this group is 0.57% (1 of 176). In addition, no relationship between CD4 cell count and food allergy was found.

DISCUSSION

The multiple immunopathogenic mechanisms involved in HIV infection are gradually being understood and are

summarized in an excellent review by Fauci.²⁸ Chronic immune system activation and an apparent predominance of TH-2 responses with a resultant cytokine profile favoring IL-4, IL-5, IL-6, and IL-10 appear to be important factors in the pathogenesis of HIV.²⁸ The reported increase in atopic disease found in people infected with HIV may result from this "immune dysregulation" responsible for the altered IgE synthesis²⁷ and the presumed increased reactivity of cells involved in allergic disease including mast cells and eosinophils.^{29,30} This theory is supported by data showing increased IgE levels in patients with HIV infection especially with progression to acquired immunodeficiency disease (AIDS).^{24-27,31} Other immunodeficiency disorders including IgA deficiency,^{1,8,9,12} graft versus host disease,² complement deficiency,¹¹ agammaglobulinemia,³⁻⁵ and various T cell disorders¹¹ are also thought to predispose patients to allergic disease including food allergy.

The estimated prevalence of adverse reactions to foods in the general population ranges from 0.3% to 27%^{32,33} with approximately 1% to 3% of chil-

Table 1. Food Allergy in Patients Infected with Human Immunodeficiency Virus

Patient No	Food(s)	Symptoms	Most Recent Event (initial event)	Skin Test	DBPCFC
1	broccoli	nausea, abdominal pain, headache	March, 1995 (July, 1994)	positive	positive
2	shellfish	urticaria	Feb, 1995 ("many years ago")	ND*	ND
3	pork	urticaria	unknown ("many years ago")	ND	ND
4	watermelon	urticaria	1978 (unknown)	ND	ND
5	almonds, peanut butter	diarrhea, headache	March, 1995 ("about 5-10 years")	ND	ND
6	fish	nausea, headache, vomiting, diarrhea	Jan, 1994 (1991)	ND	ND
7	raw fish, raw eggs	diarrhea, headache	Nov, 1994 (unknown)	ND	ND
8	shellfish	angioedema, urticaria	March, 1995 ("10 years ago")	ND	ND
9	"seafood"	anaphylaxis	"many years ago" ("since childhood")	ND	ND
10	mango	anaphylaxis	"3 years ago" ("10 years ago")	ND	ND

* ND = not done.

dren having true food "allergy."³⁴ The prevalence of food allergy in adults is unknown but appears to occur less frequently than in children. Studies of the prevalence of food allergy in adults with immunodeficiency are lacking.

Our data reveal an estimated prevalence of food allergy ranging from a minimal prevalence of 0.57% confirmed by DBPCFC to a maximal prevalence of 5.7% (patients with a strong history alone) in a group of adult patients with HIV infection. These results do not suggest a difference between patients infected with HIV (including those with severe immunosuppression) and the general population.

Although the mechanism for the increased prevalence of food allergy found in children with immunodeficiency is unknown, many authors suggest abnormal antigen processing resulting from immune dysfunction and increased penetration of food antigens after recurrent gastrointestinal infections.³⁵ Despite the frequent gastrointestinal infections seen in patients with HIV and the various evidences of immune activation including increased IgE production, our results do not suggest a clinically apparent increase in food allergy. These results coincide with a previous study that revealed a deficiency of tryptase-positive mucosal mast cells in the gastrointestinal tract of patients with AIDS.³⁶

Our patient population had some unique problems compared with the general population in that many patients were unavailable for evaluation because of severe illness. There are also several limitations to this study that are common in all studies attempting to evaluate food allergies. One problem is the self reporting of symptoms which has been shown to be a poor predictor of confirmed food allergy by DBPCFC except for immediate anaphylactic reactions.^{37,38} Despite an attempt to confirm all histories consistent with food allergy by skin prick testing (or RAST) and DBPCFC, we were unable to test many subjects including several patients with very strong histories. We included these six

patients as "positive" to give an upper limit to our estimate of prevalence. We also did not challenge patients with histories consistent with immediate anaphylactic responses to food. Although it is possible that these patients' symptoms were unrelated to a specific food or that they may have lost their sensitivity, testing of these patients may be hazardous. There is also a relatively good correlation between such histories and positive food challenges.^{37,38} RAST may have been used as a negative screening test in these three patients, but oral challenges to confirm a "positive" test to a food easily avoided in the diet were thought to be too dangerous for the purpose of this study. Despite these drawbacks, the results of such testing would not have affected our overall conclusion.

Although approximately 40% of our outpatient population did respond to the initial questionnaire, a selection bias may exist as to those who either ignored or refused to complete the questionnaire. Despite this potential, the demographics of the sampled population including CD4 cell count and patient sex are similar to our general clinic population, suggesting that if a bias did exist it did not affect characteristics related to immune suppression or sex. It should be noted that only adult patients were evaluated and it is possible that these data may not apply to infants and children infected with HIV.

Finally, our study tested only those food antigens thought to be a common cause of food allergy in adults.^{39,40} We did not test for food additives⁴¹ or spices,⁴² which may also be a cause of food allergy. It is possible that these or other food products may be contributing to an individual's symptoms, but it is unlikely that these sensitivities would dramatically change our estimate of prevalence.

In summary, it appears that although patients with HIV infection have risk factors that may predispose them to food allergy including elevated IgE production, altered gastrointestinal function due to various infections and a possible increase in other atopic dis-

orders such as drug allergy, eczema, asthma and rhinitis, they do not appear to be at increased risk of food allergy compared with previous estimates of food allergy in the general population.

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