

Unproven Diagnostic Tests for Adverse Reactions to Foods



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Date of Original Release: March 1, 2018. Credit may be obtained for these courses until February 28, 2019.

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Overall Purpose/Goal: To provide excellent reviews on key aspects of allergic disease to those who research, treat, or manage allergic disease.

Target Audience: Physicians and researchers within the field of allergic disease.

Accreditation/Provider Statements and Credit Designation: The American Academy of Allergy, Asthma & Immunology (AAAAI) is

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List of Design Committee Members: John M. Kelso, MD (author); Michael Schatz, MD, MS (editor)

Learning objectives:

1. To describe the methodology of the most commonly used unconventional tests for adverse reactions to foods
2. To reason through the potential biologic plausibility of these tests
3. To discuss with patients the evidence that these tests are unproven or disproven as diagnostic tests for adverse reactions to foods

Recognition of Commercial Support: This CME has not received external commercial support.

Disclosure of Relevant Financial Relationships with Commercial Interests: J. M. Kelso declares that he has no relevant conflicts of interest. M. Schatz discloses no relevant financial relationships.

Patients often seek opinions from allergists regarding unconventional testing for adverse reactions to foods. These tests include flow cytometry to measure the change in white blood cell volumes after incubation with foods, measurement of serum IgG or IgG₄ antibodies directed against foods, intradermal provocation-neutralization with food allergens, hair analysis, electrodermal testing, and applied kinesiology. In some cases, although the laboratory methods may be valid, there are no studies showing correlation with disease. In other cases, blinded, controlled studies have shown a lack of reproducibility and a lack of correlation with disease. Most of the tests lack biologic plausibility. By understanding the methodology of these tests and the lack of evidence supporting their utility, allergists can provide knowledgeable,

evidence-based information to patients who inquire about them. © 2017 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2018;6:362-5)

Key words: Food allergy tests; Unproven; Disproven; Controversial

It is not uncommon for patients being seen by allergists to inquire about unconventional testing for food allergy or intolerance. These tests have often been ordered by alternative medicine practitioners, but have sometimes been ordered by traditionally trained physicians as well. For some tests, patients can order the tests directly, that is, without seeing a practitioner, by mailing in test kits using home-collected dried blood spots for IgG food analysis^{1,2} or hair samples for hair analysis.³ Once the results are received, the patients often want assistance interpreting them. At other times, patients have been made aware of such tests by other people or through popular media and are asking an opinion about their usefulness. Thus, it seems appropriate for allergists to be familiar with these tests so as to be able to offer evidence-based advice regarding them. Most, but not all, websites promoting these tests are careful to specify that they are not testing for IgE-mediated food allergy but rather for various food intolerances that are often described as being late onset. The most common of these tests are reviewed here.

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No funding was received for this work.
Conflicts of interest: J. M. Kelso declares that he has no relevant conflicts of interest.
Received for publication July 14, 2017; revised August 8, 2017; accepted for publication August 18, 2017.
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2213-2198
© 2017 American Academy of Allergy, Asthma & Immunology
<http://dx.doi.org/10.1016/j.jaip.2017.08.021>

Abbreviation used
IBS- Irritable bowel syndrome

THE ALCAT TEST (CELL SCIENCE SYSTEMS, DEERFIELD BEACH, FLA)

The company's literature states that the basic principle of the test is challenging the patient's white blood cells with foods to identify those that may trigger "potentially harmful immune system reactions."⁴ The technology is described as using flow cytometry to measure the percentage change in the distribution of cell sizes at baseline and after the food challenges.⁴ They report that the percentage change in a healthy control group was less than 9% and consider a change of greater than 13% to be positive and 9-13% to be equivocal.⁵ The results are to be used to customize an elimination or rotation diet to eliminate the "specific triggers of chronic immune system activation" and alleviate various symptoms including "gastrointestinal complaints, skin diseases, neurological and mental disorders, respiratory diseases, metabolic diseases, endocrine disorders, musculoskeletal and joint disorders, immune system, and other comorbidities."⁴

A number of publications are cited on the company's website reportedly demonstrating the diagnostic utility of the test, but virtually all are abstracts as opposed to manuscripts in peer-reviewed journals. The lack of such evidence makes it impossible to objectively evaluate these claims. It may well be that the laboratory instrument being used accurately measures white blood cell volumes. However, it is unclear whether or not any changes in these cell volumes in response to food exposure would be physiologic or pathologic or how they would lead to the long and disparate list of maladies being investigated.

A critical published review of the ALCAT test concluded that although the apparatus (Coulter counter) is validated, data are not available on technical parameters of reagent quality, analytical sensitivity, measurement range, analytical specificity, precision, or accuracy nor clinical parameters of clinical sensitivity, clinical specificity, or predictive values.⁶ A more recent review agreed, stating that "the ALCAT test system is for the time being relying on unproven statements that lack scientific and clinical proofs of efficacy."⁷

IgG FOOD TESTING

Just as quantitative enzyme immunoassays can be used to measure IgE antibodies to foods, these same assays can be used to measure IgG antibodies or IgG₄ antibodies to foods. These tests are performed in many reputable laboratories, and there is no reason to doubt their validity and reliability, that is, the tests are in fact accurately and reproducibly measuring IgG antibody directed against food proteins. However, the measurement of IgG to foods is promoted to diagnose "food sensitivities" that might manifest, according to websites promoting the testing, as acne, eczema, dry and itchy skin, food intolerance, bloated after eating, fatigue, irritable bowel syndrome (IBS), joint pain, migraines, respiratory issues, weight gain and/or difficulty losing weight, ear infections, sinusitis, or urticaria.¹ Such reactions are often described as being delayed or chronic. The theories advanced on the same websites to explain how such IgG food antibodies could lead to these conditions include chronic inflammation perhaps through the formation of immune complexes.²

However, the production of IgG antibodies to foods is a normal immunologic phenomenon.^{8,9} IgG antibodies to foods are found in virtually all healthy individuals. In fact, contrary to the notion that the development of IgG or IgG₄ antibodies could lead to food intolerance, the development of such antibodies has specifically been linked to the development of food desensitization or tolerance.⁹⁻¹²

One study purporting to show the utility of specific IgG to foods as a diagnostic test retrospectively reviewed 55 patients placed on elimination of diets based on this testing because they had "complained of symptoms suggestive of adverse food reactions" and had shown elevated IgG titers to foods.¹³ The symptoms could include "malaise, prostration, fever, rash, arthritis, gastrointestinal symptoms, neurological symptoms, lymphadenopathy, myocardial ischemia, or transient renal disease." A total of 31 patients chose to follow the diet and were compared with 24 patients who did not. Of the 31 who followed the diet, 28 were clinically improved based on clinical interviews compared with 7 of 24 who did not. This study demonstrates the flaws found in most studies of this and other unproven tests for food intolerance. It did not include a control group, for example, of subjects who made dietary changes not based on IgG testing. The study was retrospective, not randomized or blinded, evaluated a broad array of symptoms and conditions unlikely to have a common pathophysiology, and used ill-defined and subjective measurements of improvement.

The proposed utility of food elimination diets based on IgG food antibody testing has also been evaluated in patients with IBS.¹⁴ A total of 150 patients with IBS were randomized to a 3-month (true) diet that either excluded foods to which they had elevated IgG antibodies or a control (sham) diet that excluded a similar number of foods but not those to which they had elevated IgG antibodies. Those on the true diet had a small (10%) but statistically significantly greater reduction in symptoms than those on the sham diet. However, the study was criticized because the particular foods eliminated in very high percentages in those on the true diet such as milk, egg, and wheat were eliminated in much smaller percentages in those on the sham diet; instead, an appropriate control diet would have eliminated the same foods irrespective of the IgG antibody level.¹⁵

A position paper by the European Academy of Allergy and Clinical Immunology,⁸ endorsed by the American Academy of Allergy, Asthma and Immunology,¹⁶ states that "food-specific IgG₄ does not indicate (imminent) food allergy or intolerance, but rather a physiological response of the immune system after exposition to food components. Therefore, testing of IgG₄ to foods is considered as irrelevant for the laboratory work-up of food allergy or intolerance and should not be performed in case of food related complaints." A position statement from the Canadian Society of Allergy and Clinical Immunology concludes that "positive test results for food-specific IgG are to be expected in normal, healthy adults and children. Furthermore, the inappropriate use of this test only increases the likelihood of false diagnoses being made, resulting in unnecessary dietary restrictions and decreased quality of life."¹⁷

PROVOCATION-NEUTRALIZATION TESTING

In this procedure, food sensitivities are identified by intradermal injection of extracts of suspected foods in an attempt to provoke previously reported food-related symptoms. A different

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