

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

dose of the offending allergen is then injected to “neutralize” the reaction.^{18,19}

It is conceivable that exposure to a food to which a patient is “intolerant” by intradermal injection could provoke symptoms, although this seems unlikely given the small amounts injected. It does not, however, seem biologically or immunologically plausible that within this short time frame injection of the same substance could somehow “neutralize” such a reaction.

In a double-blind study of this technique, 18 patients who had previously been reported to have reacted to specific food substances were evaluated in the offices of physicians experienced with the technique by injection of either the suspect food or saline in random order.¹⁸ Patients were then asked to state whether the injection had been the food to which they were sensitive or saline. They responded positively to 27% of the food injections and to 24% of the saline injections. When the neutralizing doses were administered after reactions, they were just as likely to be effective whether the food or saline was injected. The authors concluded that “when the provocation of symptoms to identify food sensitivities is evaluated under double-blind conditions, this type of testing, as well as the treatments based on ‘neutralizing’ such reactions, appears to lack scientific validity. The frequency of positive responses to the injected extracts appears to be the result of suggestion and chance.”

In another study, 132 patients with suspected food or chemical sensitivities underwent double-blind intradermal injections of foods or chemicals or saline in random order.¹⁹ Seventy percent of the patients reported symptoms to saline injections. Reactions to foods, chemicals, and saline occurred in a random pattern. The authors concluded that “skin tests that rely on the provocation of symptoms to determine whether a patient is sensitive should not be used to make diagnostic or therapeutic decisions.”

HAIR ANALYSIS

The website of one company offers hair analysis as a means of evaluating intolerances to hundreds of food and non-food items.³ Although the laboratory methodology is not described, they explain that the hair samples are checked against a database and “those displaying an intolerance of 85% and over...typically trigger intolerance symptoms within the body” that could include “headaches, nausea, bloating, stomach cramps, diarrhea, constipation, fatigue, skin disorders, brain fog, lethargy or constant tiredness.” They state that changing one’s diet based on the results can alleviate these symptoms.

There are no published studies regarding the outcome in patients who have altered their diets based on hair analysis for food intolerance. However, in one study, hair samples from 9 nonallergic subjects who “were not aware of any sensitivity reactions to food or any other substances” were sent in duplicate to 3 different laboratories offering hair analysis for food intolerances where the authors found a “striking...frequency with which positive tests were reported often with discrepancies between matched samples.”²⁰ They concluded that “the results gave clear evidence of diagnostic failure, lack of reproducibility, and a remarkably high number of reports suggesting that unsuspected allergies were present in [the controls].”

ELECTRODERMAL TESTING (EG, VEGA TEST)

In this technique, patients hold an electrode in one hand and another electrode is placed somewhere else on the patient’s body,

often an acupuncture point, although there is no puncturing of the skin. An electrical circuit exists between the 2 electrodes to which a small voltage is applied. Also within the electrical circuit, but not touching the patient, are glass vials containing test substances, and skin impedance is measured in arbitrary units.²¹⁻²³ In addition to assessing for food “sensitivities,” some practitioners promote this testing as a substitute for IgE testing,²⁴ which could pose a danger if truly allergenic foods are reintroduced in the diet. There are no studies evaluating this technique for food sensitivities, but 2 studies have compared it with conventional tests for airborne allergens.

In one study, 15 patients who had had positive prick skin tests for dust mite or cat and 15 with negative skin tests underwent electrodermal testing by 3 different experienced operators with 18 samples containing extracts of dust mite or cat dander or distilled water in random order in a double-blind fashion.²² Approximately 25% of all tests were “positive,” whether allergens or water were tested and whether the subjects were skin test positive or not. All 3 operators had equally poor results. The authors concluded that “electrodermal testing could not distinguish between atopic and nonatopic participants.”

In another study, 72 patients with allergic rhinitis and/or asthma and positive skin tests and serum-specific IgE to common aeroallergens as well as 28 healthy subjects with negative skin tests and serum-specific IgE underwent double-blind electrodermal testing by an experienced operator with vials containing histamine, allergens, or normal saline. There was no reproducibility of observations with the same test substance in the same individual and no relationship between the skin conductivity measurements and the substance in the vial. They concluded that electrodermal testing “cannot correctly detect respiratory allergy” and that “those who manufacture or use electrodermal instruments should always refer to rigorous well-controlled data before claiming for the efficacy of the method.”²³

APPLIED KINESIOLOGY

In this test, food sensitivities or intolerances are evaluated by having the patient hold a vial containing the test food in one hand while the contralateral arm is extended. The practitioner then applies downward pressure to the extended arm and evaluates for weakness, which would demonstrate a sensitivity to the food being tested.²⁵

In one study of this technique, patients were evaluated with 12 labeled vials containing extracts of different foods.²⁵ If the tester indicated that there was a positive response to one or more of the labeled vials, they were asked to also evaluate blinded vials that contained either food extracts or saline. With the labeled vials, 6 patients gave a positive reaction to milk, but when these 6 patients had 12 blind challenges with milk, only 1 gave a positive result. Among 14 patients who gave negative results to milk with the labeled vials, there were 4 positive reactions on blind testing. Altogether, 16% of blind tests gave positive results among those with positive results on open testing and 16% gave positive results among patients who had negative results on open testing. Saline solution caused positive reactions in 18%. The analysis showed concordance with duplicates similar to that expected by chance.

In another assessment of this methodology, 51 subjects were tested in 3 separate trials, first by 2 different kinesiologists and in a third trial by a hand dynamometer to objectively measure grip strength.²⁶ Each subject in each trial was tested, in random

order, with one vial containing normal saline and another vial containing hydroxylamine hydrochloride (NH₃OH), a corrosive irritant/toxin. Overall, the toxic substance was correctly identified 53% of the time, about what would be expected by chance. Similarly, the results for the 2 kinesiologists and the hand dynamometer were almost exactly at chance.

Finally, a literature review of applied kinesiology concluded that “there is insufficient evidence for diagnostic accuracy with kinesiology, the validity of muscle response and the effectiveness of kinesiology for any condition.”²⁷

APPROACH TO PATIENTS

Many patients suffer from physical, psychological, and psychosomatic conditions for which conventional medicine cannot provide diagnosis or treatment. Such patients understandably turn to practitioners who tell them that these ailments are the result of ingestion of certain foods that can be identified by the testing methods described above and that dietary manipulation based on the results will relieve their symptoms. Many patients feel better because they feel like they have an explanation for their illness. The placebo effect is very powerful. Patients may feel better after dietary changes for a variety of reasons unrelated to their test results. Although it is important to be sympathetic with these patients, as scientists, it is also important for us to gently explain that these tests have not been validated by science. Such patients are less likely to be won over by dismissal of the tests as quackery than by statements that might begin, “Well, as it turns out, studies of these tests have shown....” There are several potential detriments to the use of such tests including nutritional deficiencies if certain foods are avoided and dangerous reactions if foods to which the patient has a true hypersensitivity response are consumed. Further, such testing and consultation with these practitioners is often expensive and typically not covered by health insurance, and thus patients may have a financial stake in the tests. If, despite our explanations to the contrary, a patient believes strongly in such testing and it will not result in an adverse financial or health outcome, it may be best to simply acknowledge that there are many things in medicine we do not fully understand. All we can do is firmly state our case and respect the patient’s autonomy.

CONCLUSIONS

The unconventional tests for food allergy described here are unproven, or in many cases disproven, techniques. Most lack biologic plausibility and none has been demonstrated in appropriate studies to correlate with disease. Until such time as those who promote these tests can demonstrate their utility in appropriate scientific studies, their use cannot be endorsed. Patients seeking counseling regarding these tests should be advised as to the lack of scientific support for them, and in many cases studies disproving their utility, as well as the potential dangers of dietary manipulation based on the results.

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