Laboratory Food Allergy Testing: Evaluating the Necessity for this Diagnostic Approach

by Daniel Ko

Headaches, arthritis, joint pain, depression, fatigue, hypoglycemia, recurrent infections, mood swings, acne, eczema, irritable bowel syndrome (IBS), and attention deficit disorder (ADD). These are just some of the health problems many individuals and some doctors attribute to hidden food allergies or food hypersensitivity. However, with food allergy being the most commonly self-diagnosed health problem in the United States, the search for a standardized way of approaching the question of allergy tests is underway.1

"Food allergy is usually over-diagnosed by the public, often under-diagnosed by physicians, and may be misdiagnosed by allergists," says Sami Bahna, MD, DrPH, Professor of Pediatrics & Medicine, and Chief of Allergy & Immunology Section, Louisiana State University Health Sciences Center, Shreveport, Louisiana.

Food allergies affect approximately 2% of the general US population and seem to be increasing in prevalence.2 If, in fact, certain people have sometimes severe allergic reactions – including anaphylaxis – to various foods, then reducing or eliminating exposure to these foods would be essential for achieving optimal health.

The debate, however, is how to accurately determine which foods one is sensitive to. The current gold standard for food-allergy testing is through an elimination diet followed by a carefully monitored oral food challenge.3 In addition to being time-consuming and inconvenient since challenge testing carries a risk of serious reaction, only trained professionals can perform them, and emergency treatment must be immediately available in case it is needed.

In light of this, reviewing the scientific evidence behind some other methods currently used to test for food allergies is worthwhile. These include food symptom diaries, measuring food-specific IgE antibody levels using skin prick tests, radioallergosorbent (RAST) testing, or enzyme-linked immunoassay (ELISA), measuring IgE levels, and the antigen leukocyte cellular antibody test (ALCAT).

Symptom Diaries

Every doctor would probably agree that patients suspected of having a food allergy should have a detailed health history taken and a thorough physical exam performed by a qualified professional. This type of diagnostic evaluation may also include symptom diaries, specific screening tests such as skin testing or antibody assays, and confirmation by challenge testing.4

The difficulty with just using symptom diaries, however, is distinguishing between food allergies and food intolerances. A food allergy, or hypersensitivity, represents an aberration of the normal immune response to food protein, whereas food intolerance does not involve immune mechanisms.5 The classic example of food intolerance is the bloating and other digestive system complaints that result from a lack of the enzyme lactase needed to digest dairy sugar lactose. Other individuals may experience similar symptoms because their immune system makes antibodies to milk proteins. Because the symptoms of food allergy and food intolerances often overlap, a proper and thorough evaluation is essential. Moreover, since both concepts are under the umbrella term of "adverse food reactions," one should be aware of other categories belonging to this same group. They include food poisoning, psychological reactions to food, and carbohydrate malabsorption. Food allergies are divided into IgE-mediated (both immediate and late phase) and non-IgE mediated reactions.6

Measuring IgE levels

IgE antibodies are important in the development of the allergic response, and are found in high concentrations in individuals with asthma, atopic dermatitis, hay fever, and classical food allergy reactions. Although skin testing for IgE antibody is simpler, more sensitive, cost-effective, and has a better correlation to clinical symptoms, it may not be suitable for certain patients. In light of this risk, RAST or one of its various analogues should be considered in particular patients. For example, those with a history of severe life-threatening food reactions, young infants with poor skin reactivity, individuals with severe generalized eczema, and those with an inability to discontinue antihistaminic medications are good candidates for serum IgE antibody testing.

As with food diaries, however, there is a level of ambiguity in interpreting IgE test results. Although positive results indicate that IgE is present, they don't necessarily mean that an individual will react when he or she ingests that particular food. Some people even outgrow their food allergies and still test positive for IgE for many years.7

Another factor that complicates matters with IgE testing is the potential for cross-reactivity and non-specific reactions. An array of foods can contain similar allergenic proteins, such as pollen. For example, a person allergic to peanuts could test positive for soy allergy, despite not having symptoms of soy allergy, and total IgE levels can be elevated in several non-allergic conditions.8

Conversely, normal serum total IgE levels don't exclude the presence of undetected allergies because specific IgE testing is what matters. Some other reasons for falsely-negative IgE test results include a pathophysiological, cell-mediated cause to the reaction, testing of the wrong foods, or the test simply not being sensitive enough. In fact, the majority of gastrointestinal food hypersensitivity disorders are not mediated by IgE antibody, and so evaluation and detection of these sensitivities is much more accurate with elimination diets, selected oral food challenges, and biopsies as indicated.9

However, a more accurate IgE test has been developed by Pharmacia-Upjohn Diagnostics (Uppsala, Sweden). Their quantitative CAP-system fluorescent enzyme immunoassay for IgE antibodies may provide more useful positive and negative predictive values than previous RAST and ELISA.10,11

Diagnosis of Non-IgE Mediated Food Allergy

A growing body of evidence is supporting the notion that T-lymphocytes play a crucial role in the pathophysiology of non-IgE mediated
food allergies. Some novel approaches to testing for T-lymphocyte-mediated food allergies that have yet to be rigorously evaluated include patch testing, measurement of cytokine production by lymphocytes after stimulation with food allergens, and measurement of cytokines and eosinophil activation markers in the stool.12

Some tests that are widely discouraged by food allergy experts include measurement of IgG4 antibody and provocation-neutralization (drops placed under the tongue or injected under the skin to diagnose and treat various symptoms), and applied kinesiology.13

Use of “alternative” Lab Tests to Detect Food Allergies

If IgE testing can be ambiguous, or not highly reliable indicators for hidden or delayed food allergy problems,14 one must question the reliability and validity of “alternative” lab tests.

A statement issued by participants of the Pediatric Food Allergy Symposium, sponsored by the Food Allergy and Anaphylaxis Network and the Jaffe Food Allergy Institute of the Mount Sinai School of Medicine, New York, and held on April 20, 2002, officially advised against the use of these tests for screening and diagnostic purposes because of their limitations and the potential for false results. The participants urged that, in most cases, the diagnosis of food allergy requires the use of diagnostic elimination diets and physician-supervised oral food challenges.

Measuring IgG levels

Despite the recommendations of participants of the Pediatric Food Allergy Symposium, some laboratories test for IgG antibodies. The belief is that these antibodies primarily mediate late-onset (delayed) hypersensitivity reactions, which some say are more common than immediate food allergy reactions. These assays are based on the findings that some IgG subclasses have been associated with in vitro degranulation of basophils and mast cells, complement cascade activation, and high concentrations of some serum IgG subtypes in certain atopic individuals.15 However, this is an extrapolation that IgG to food antigens correlates to signs and symptoms of food allergy. At least one lab offering IgG testing stresses to its clients that an elimination diet followed by a gradual reintroduction of suspect foods remains the gold standard in establishing relationships between antigenic exposure and clinical symptoms. They acknowledge, however, that these diets can be extremely burdensome and overwhelming for patients. The literature of some IgG test manufacturers includes the disclaimer that assessment of relative IgG antibodies to a wide variety of foods using ELISA can provide “a comfortable starting point for dietary manipulation and therapy by identifying those foods against which the patient is producing antibodies.”

Other reports have demonstrated a poor correlation between IgG antibody-detection techniques and disease states.16 The presence of IgG antibodies appears primarily to indicate prolonged exposure to a particular food and is a

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normal physiological response. Individuals without food allergies and children developing a tolerance to particular foods often have increased IgG antibody titers to that food. Moreover, high IgE levels can stimulate the production of IgG and IgG4 autoantibodies against IgE that can be mistakenly identified in immunoassays as food-specific. Therefore, testing for food-specific IgG can be expensive as well as unreliable. It may yield more confusion than clarification.

Other Issues Raised About IgG-ELISA Testing for Food Sensitivities

Several doctors have expressed concerns regarding IgG testing. They include:13,14

1. A lack of intra-laboratory reproducibility

2. Doubtfulness concerning the role of IgG food-specific antibodies in the pathophysiology of adverse reactions to food, as IgG antibodies have been shown to play a blocking or protective role in many instances. Hence, there are a lot of false positives.

3. The likelihood that many adverse reactions to food are pharmacologically mediated and thus not detectable through immunological assays.

4. The observed reactivity may be due to contaminants in the food (such as bacteria or fungi) rather than the food itself.

5. The process of digestion alters the composition of food and therefore likely its allergenicity.

ALCAT System

Another method of allergy-detection available to doctors and patients is the ALCAT test. This system is designed to individually test samples by incubating food extracts with the patient's whole blood, and then analyzing for changes in cell count and size under controlled conditions. Computer analysis compares volumetric changes in the white blood cells to the control curve. The theory here is that changes in leukocytes reflect activation of the cell or effects secondary to the action of immune factors, mediators, or regulatory substances upon the cells.

However, at least one expert has argued the physiologic basis for using the ALCAT is not sound. Even the test's manufacturers note that further work needs to be conducted to elucidate the mechanism behind the test. However, they maintain that ALCAT can identify potentially offending foods in patients suspected of having food sensitivities. Furthermore, they say it can also be useful in patients who have attempted elimination diets but are unable, upon food challenges, to adequately or clearly identify the unsafe foods.

The proponents of this approach say that ALCAT test results can be used by physicians to select the foods that can be eliminated and thereby avoid routine and arbitrary elimination diets. They argue that by using the ALCAT as a precursor to elimination testing, patients can avoid excluding many common and "safe" foods and make this form of testing more palatable. Some physicians say they are satisfied with the results they are getting with ALCAT. A few studies have also documented the reliability of using the ALCAT to identify reactions to food additives. In one particular study, the overall correlation between ALCAT test results with a double-blind challenge was 83.4% for identifying unsafe foods in patients with evidence of food sensitivity. However, overall there is little evidence supporting its use as part of a diagnostic work-up for food allergies.

Conclusion

Alternative lab tests such as the ALCAT system or measuring IgG will likely continue to be the subject of debate. The serum tests are convenient because conventional approaches such as skin testing are still a specialized tool that many physicians can't easily incorporate into their office routines. Furthermore, the labs that conduct these tests often include a suggested "rotation" or "elimination" diet along with a report of foods the patient is allergic to. Rotation diets, however, are not specific. It is crucial for the particular offending food to be accurately identified and strictly avoided.

However, in the meantime, food allergy tests can be used as a starting point for identifying reactive foods. A positive test on its own correlates with an adverse reaction less than 50% of the time and, in many circumstances, positive results are "false positives." Moreover, patients suspected of having food allergies should also be investigated for hormonal changes, GI disorders, exercise, intercurrent illness, and emotional stress that may be causing similar symptoms.

Although there are numerous anecdotal reports of success with these 'alternative' lab tests, there is still very little scientific evidence to support their use.

References


19. Personal communication with Rudy Rivera, MD, private practice, Palm, Texas.

