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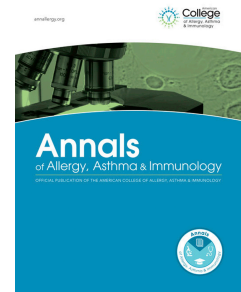
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IgG Food Testing

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1 Patients often present to allergy clinic with a history of diverse, multi-system symptoms.
2 Convinced that they have food allergies, they seek testing and evaluation. However, many
3 patients present to clinic having already completed commercially available food allergy or
4 sensitivity tests that have become commonplace in popular media. The majority of these tests are
5 immunoglobulin G (IgG) food panel testing, with up to 100 foods evaluated with a single test.
6 The companies claim to diagnose food sensitivities or intolerances based solely upon elevated
7 IgG levels to foods. Often described as “delayed onset reactions,” these food intolerances are
8 purported to present with a myriad of symptoms, including bloating, joint pain, migraines, or
9 acne. When evaluating patients with undifferentiated complaints who are convinced of food
10 allergy, the allergist is often in a position where patience, empathy, and communication skills are
11 more valuable assets than technical knowledge. Still, it must be recognized that food allergies
12 and food intolerances are widespread conditions, with food allergies affecting 5-10% of the
13 population, and food intolerances affecting up to 20% of the population.

14
15 The terms food allergy, food intolerance, and food sensitivity have been used erroneously and
16 interchangeably by healthcare practitioners and the public. Clarity and precision are essential,
17 especially with respect to potentially life-threatening manifestations. Food allergies are
18 immunologic, adverse reactions to foods that can be IgE-mediated, non-IgE-mediated, or mixed.
19 An IgE-mediated, Type I hypersensitivity to food can present with acute onset of anaphylaxis,
20 hives, respiratory, cardiovascular, and/or gastrointestinal symptoms. Non-IgE mediated or mixed
21 IgE-mediated allergies include eosinophilic esophagitis, food protein induced enterocolitis, and
22 allergic proctocolitis. In contrast, food intolerances and food sensitivities are nonimmunologic
23 reactions. Food intolerances refer to difficulty digesting or metabolizing certain foods. Food

sensitivities describe a wide range of symptoms that are attributed to food based on experience and beliefs.

Not surprisingly, food-specific IgG is present in nearly all healthy individuals. IgG is an antibody that develops in response to antigen exposure and plays a role in immunologic memory. In fact, IgG and IgG4 antibodies are associated with food tolerance or desensitization, rather than a sensitivity. IgG4/IgE ratios are significantly higher in peanut consumers as opposed to peanut avoiders.¹ Moreover, there are no established reference values for food-specific IgG testing, and wide variability exists among the general population. Although IgG food tests performed at certified laboratories likely report accurate values, the clinical significance of a reportedly elevated food-specific IgG remains controversial.

Another issue with commercial food IgG testing is that instructions for food elimination or restriction diets, especially for foods with higher IgG antibody levels, often accompany the testing report. Currently, there is no clear evidence that elimination diets based on food-specific IgG testing have been beneficial in symptom reduction. One oft-quoted study retrospectively reviewed 55 patients who were placed on elimination diets based upon IgG testing results.² Patients were screened for symptoms including: malaise, prostration, fever, rash, arthritis, gastrointestinal symptoms, neurological symptoms, lymphadenopathy, myocardial ischemia, or transient renal disease. Twenty-eight of 31 patients (90%) who chose to make dietary changes based on IgG testing had subjective improvement of symptoms, compared to 7 of 24 patients (29%) who did not pursue an IgG-guided diet. In addition to being a retrospective study, this

study was limited in validity due to lack of randomization or blinding and use of subjective outcome measures.

Another study evaluated the effectiveness of food elimination diets based upon IgG food testing in patients with irritable bowel syndrome (IBS).³ In a randomized, controlled trial of 150 people diagnosed with IBS, patients who followed a diet directed by IgG testing for 12 weeks had a 10% decrease in IBS symptom scores as compared to patients following a sham diet (i.e. excluding a similar number of foods, but unrelated to those with elevated food-specific IgG levels). However, one inconsistency in the study is the control group did not eliminate certain allergenic foods such as milk, eggs, and wheat to the same extent as the experimental group. A better study design would be to randomize subjects with comparable levels of IgG to allergenic foods to an elimination diet or sham diet group.

While other randomized controlled trials have demonstrated an inconsistent benefit of using IgG food-specific elimination diets in patients with migraine headache symptoms, these studies are limited by the low number of patients. Some preliminary data involving a small group of adult patients with eosinophilic esophagitis suggest that food-specific IgG testing have a role in the assessment and management of eosinophilic esophagitis.⁴ The predictive ability of IgG4 remains undefined and further work will be needed to better understand the positive and negative predictive values of these tests in the clinical management of eosinophilic esophagitis.

IgG food testing and associated elimination diets can lead to burden and negative health consequences. IgG food testing is rarely covered by insurance and can cost hundreds of dollars.

69 Additionally, elimination diets can cause significant nutritional deficiencies. Elimination or
70 restriction of allergenic foods, especially in those with history of atopic disease or food
71 sensitization (i.e. positive food-specific IgE testing without clinical history) can lead to loss of
72 tolerance and development of IgE-mediated food allergy.¹ One study demonstrated up to 20% of
73 children with atopic dermatitis who had no prior history of immediate reactions to food can
74 progress to develop systemic allergies, with 30% of those children developing anaphylaxis with
75 reintroduction after dietary elimination.⁵

76
77 Given the limited evidence, several organizations including the American Academy of Allergy,
78 Asthma & Immunology and the European Academy of Allergy and Clinical Immunology
79 recommend against the use of IgG testing for diagnosis of food allergies or food intolerances.
80 Although preliminary studies regarding the use of food-specific IgG testing show some promise
81 in irritable bowel syndrome, migraines, and eosinophilic esophagitis, larger, double-blinded
82 randomized controlled studies are needed to determine clinical validity of these tests.
83 Elimination diets carry significant risks, including development of nutritional deficiencies and
84 food allergies. Given the limited value of IgG food testing, allergists would benefit most from
85 obtaining a careful history and physical examination to guide management of adverse food
86 reactions.

1. Du Toit G, Roberts G, Sayre PH, et al. Randomized Trial of Peanut Consumption in Infants at Risk for Peanut Allergy. *N Engl J Med*. 2015;372(9):803-813. doi:10.1056/nejmoa1414850
2. Marinkovich V. Specific IgG antibodies as markers of adverse reactions to foods. *Monogr Allergy*. 1996;32:221-225.
3. Atkinson W, Sheldon TA, Shaath N, Whorwell PJ. Food elimination based on IgG antibodies in irritable bowel syndrome: A randomised controlled trial. *Gut*. 2004;53(10):1459-1464. doi:10.1136/gut.2003.037697
4. Wright BL, Kulis M, Guo R, et al. Food-specific IgG4 is associated with eosinophilic esophagitis. *J Allergy Clin Immunol*. 2016;138(4):1190-1192.e3. doi:10.1016/j.jaci.2016.02.024
5. Chang A, Robison R, Cai M, Singh AM. Natural History of Food-Triggered Atopic Dermatitis and Development of Immediate Reactions in Children. *J Allergy Clin Immunol Pract*. 2016;4(2):229-236.e1. doi:10.1016/j.jaip.2015.08.006