Immunoglobulin G and Food Allergies: Beyond the Controversy

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Abstract *Adverse reactions to food, such as allergies or intolerances, are relatively common. Current medical practice relies primarily on testing for immunoglobulin E (IgE) reactions to identify specific food allergies. However, IgE is involved in acute allergic reactions, and it has limited usefulness for diagnosing chronic non-acute food allergies. In contrast, immunoglobulin G (IgG) reactions take longer to develop and are not usually acute. IgG levels may increase as a consequence of intestinal permeability. For example, gliadin (found in gluten) breaks down tight junctions (TJs), which are protein complexes that line the GI tract. When TJs break down, intestinal permeability (leaky gut syndrome) increases, allowing incompletely digested proteins to enter the bloodstream and trigger an IgG-based autoimmune reaction. Not surprisingly, IgG levels are often elevated in patients with celiac disease and non-celiac gluten sensitivity. Other diseases, including mood disorders and irritable bowel syndrome, also appear related to IgG-mediated food reactions. While IgG testing may be controversial, it remains an important tool for identifying chronic, non-acute food allergies.*

Introduction

Adverse symptomatic reactions to foods affect an estimated 4 to 6 percent of children and 2 to 4 percent of adults in Westernized societies. These food reactions are now recognized as a growing problem in developed nations.[1,2] Often referred to as "food allergies," these reactions may result from a breakdown of the immune-modulated oral tolerance to food. Such tolerance is normally necessary to suppress immune responses to "foreign" substances entering the body through the gastrointestinal tract.[2]

Unfortunately, the medical testing of food sensitivities has been characterized by a lack of consistency, and no widely accepted criteria exist for diagnosing food allergies.[3] Part of the diagnostic problem is that symptomatic food reactions can mimic or exacerbate different physical or psychiatric disorders. This potential diversity of symptoms can make the diagnosis of food allergies difficult: for example, clinicians might make a symptomatic diagnosis of irritable bowel syndrome (IBS) or depression, while food allergies might be the underlying cause of those symptoms in some patients.

Further complicating the situation, symptomatic reactions can be caused by a variety of factors, including a "true allergy," e.g., immunological responses (IgE and non-IgE); a non-allergic food sensitivity; or a food intolerance. It is likely that additional mechanisms, both immunological and non-immunological, will be identified as causes of symptomatic food-related reactions. The identification of food allergies will remain important because it differentiates between foods that can trigger adverse reactions and those that do not trigger reactions.

The use of immunoglobulin G (IgG) to identify food allergies has been controversial. Current medical practice relies primarily on testing for immunoglobulin E (IgE) to identify food allergies. However, IgE is responsible for acute allergic reactions, but it has limited usefulness in terms diagnosing chronic non-acute food allergies. In contrast, IgG reactions take longer to develop and are not usually acute.[4,5] Because of its limitations, the use of only IgE testing might significantly underestimate the prevalence of food allergies. In addition, there is also a possibility that IgG I-IV might function, at least some of the time, as "blocking antibodies" that prevent immediate responses by inhibiting IgE.[5]

A recent paper by Karakula-Juchnowicz explored the role of "IgG food hypersensitivity" as a consequence of the breakdown of tight junctions (TJs). TJs are protein complexes that line the gastrointestinal tracts, and they serve as a gateway that either enables or blocks the passage of nutrients through the GI barrier and into the bloodstream. TJs also influence the body's immune tolerance and response to antigens. As one example, zonulin regulates the permeability of TJs, and in some people zonulin is over-produced as part of the reaction to the protein gliadin (found in gluten). The over-production of zonulin uncouples the tight barrier of TJs, increasing gut-wall permeability (i.e., leaky gut syndrome).[6-11] This situation enables relatively large molecules to enter the bloodstream and potentially trigger an IgG response.[4,12] Not surprisingly, IgG levels are often elevated in patients with celiac disease and non-celiac gluten sensitivity.[13] In addition, pro-inflammatory cytokines, oxidative stress, and the pro-inflammatory transcription factor nuclear factor kappa beta can also damage the normal functioning of TJs.

Karakula-Juchnowicz is one of a number of physicians who has suggested that depression may sometimes involve an inflammatory food reaction, which can sometimes be confirmed with IgG testing.[4] In fact, a small number of physicians, dating back to the 1970s and 1980s, used the term "cerebral allergies" to describe how food sensitivities sometimes had psychiatric effects.[14]

Carr described the case history of a young girl who had for years eaten a gluten-free diet because of health problems. At age 10, however, she consumed a gluten-containing diet for one week and quickly developed depression and suicidal thoughts. Her parents resumed the girl's gluten-free diet, and her depression started to resolve within a few days. The Profile of Mood States questionnaire found that her mood disturbance score decreased from 154 to 12 during this time.[15] Other research supports the idea that gluten consumption can cause depression-like symptoms in patients with nonceliac gluten sensitivity. In a placebo-controlled study of 22 patients with IBS, Peters reported that a three-day exposure to gluten resulted in feelings of depression.[16]

A clinical trial by Atkinson found IgG testing useful in patients diagnosed with IBS. She found that IgG testing identified sensitivities to numerous foods in the patients, particularly yeast, milk, whole egg, wheat, cashew nuts, and peas. After following a diet that eliminated the suspect foods, the IBS patients had an average 10 percent reduction in their symptoms. The IBS patients who were fully compliant with the elimination diet had an average 26 percent reduction in symptoms. When the subjects became less compliant with the diet, they developed an average 24 percent deterioration of IBS symptoms.[17]

A recent detailed case history by Anderson described a patient diagnosed with multisite muscle fasciculations (involuntary muscle twitching). The patient, a 28-year-old man, had been diagnosed with wheat allergy at age 24 but had not followed a gluten-free diet. The fasciculations began in his eye and then involved his lips and legs. He also developed GI problems, fatigue, and "brain fog." IgG testing identified sensitivities to numerous foods, particularly to wheat gluten, whole wheat, milk, whey and other dairy products, rye, spelt, chicken egg yolk, chicken egg white, and duck egg white. In less than six months of following a diet that

eliminated the food sensitivities, the patient's muscle fasciculations resolved. In addition, he experienced a reduction in his brain fog, fatigue, and GI disturbances.[18]

In conclusion, the diagnosis of food allergies is currently limited by current methods of testing. Mullin observed that while IgE-based testing remains the gold standard for confirming the presence of food allergies, "immunoglobulin G (IgG)-based testing showed promise, with clinically meaningful results. It has been proven useful as a guide for elimination diets, with clinical impact for a variety of diseases."[19] Unfortunately, while IgE tests are useful for acute reactions, they have limited value in identifying other types of adverse food reactions. While IgG testing may be controversial, it remains one of the tools currently available for identifying chronic, non-acute food allergies. One of its clinical benefits is that it can help patients identify and consume "safe" foods while avoiding "unsafe" foods.

Competing Interests

The authors declare that they have no competing interests.

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