Cambridge Nutritional Sciences
Evidence-Based Clinical Relevance of Food Specific Serum IgG Antibodies
References
References against IgG Testing

Despite the large volume of published works implicating IgG mediated immune responses as part of the aetiology of these complex diseases, the clinical utility of specific food IgG antibody measurements has been called into question. Typically position statements issued by various allergy societies are cited as evidence for this view. In almost all cases the source for these statements comes from the Joint Task Force on Practice Parameters, representing the American Academy of Allergy, Asthma & Immunology (AAAAI); the American College of Allergy, Asthma & Immunology (ACAAI); and the Joint Council of Allergy, Asthma & Immunology (JCAAI).


Summary Statement 9: Manage non–IgE-mediated reactions to foods with appropriate avoidance and pharmacotherapy as indicated with the understanding that the specific role of immunity (eg, IgA, IgM, IgG, and IgG subclasses) in these forms of food allergy has not been demonstrated. [Strength of recommendation: Strong; B Evidence]

Delayed gastrointestinal reactions include eosinophilic esophagitis (EoE), eosinophilic gastroenteritis, eosinophilic proctocolitis, and food protein–induced enterocolitis syndrome (FPIES). Delayed type hypersensitivity reactions can be triggered by many foods but most commonly cow’s milk, soy, wheat, and egg.

The role of IgG was not discussed in this section at any point with no specific references to IgG measurements cited.

Summary Statement 34: Unproved tests, including allergen specific IgG measurement, cytotoxicity assays, applied kinesiology, provocation neutralization, and hair analysis, should not be used for the evaluation of food allergy. [Strength of recommendation: Strong; C Evidence]

Insufficient evidence exists to support the use of a number of unproved or non-standardized procedures and tests. Examples of unproved methods include allergen-specific IgG measurement, cytotoxicity assays, applied kinesiology, provocation neutralization, hair analysis, lymphocyte stimulation, gastric juice analysis, measures of specific IgA levels, HLA screening, type III immune complex levels, and others. These tests should not be used because results can lead to misdiagnosis or missed diagnosis of IgE-mediated food allergy, thus leading to inappropriate or unnecessary dietary elimination of foods. Such testing can also result in delay of appropriate diagnostic evaluation and management of IgE-mediated food allergy.

This statement is simply making the very important point that IgG testing should never be confused with IgE allergy testing and that it is imperative that this distinction is apparent when discussing the clinical utility of such test or when assessing a patient’s medical history to determine which testing may be appropriate. There are 3 references cited, one is regarding the use of IgG4 specifically and none are for the use of IgG.
References to Support IgG Testing


INTRODUCTION: It is well-known that specific foods trigger migraine attacks in some patients. We aimed to investigate the effect of diet restriction, based on IgG antibodies against food antigens on the course of migraine attacks in this randomised, double blind, cross-over, headache-diary based trial on 30 patients diagnosed with migraine without aura.

METHODS: Following a 6-week baseline, IgG antibodies against 266 food antigens were detected by ELISA. Then, the patients were randomised to a 6-week diet either excluding or including specific foods with raised IgG antibodies, individually. Following a 2-week diet-free interval after the first diet period, the same patients were given the opposite 6-week diet (provocation diet following elimination diet or vice versa). Patients and their physicians were blinded to IgG test results and the type of diet (provocation or elimination). Primary parameters were number of headache days and migraine attack count. Of 30 patients, 28 were female and 2 were male, aged 19-52 years (mean, 35 +/- 10 years).

RESULTS: The average count of reactions with abnormally high titre was 24 +/- 11 against 266 foods. Compared to baseline, there was a statistically significant reduction in the number of headache days (from 10.5 +/- 4.4 to 7.5 +/- 3.7; P < 0.001) and number of migraine attacks (from 9.0 +/- 4.4 to 6.2 +/- 3.8; P < 0.001) in the elimination diet period.

CONCLUSION: This is the first randomised, cross-over study in migraineurs, showing that diet restriction based on IgG antibodies is an effective strategy in reducing the frequency of migraine attacks.


OBJECTIVES: To evaluate therapeutic potential of the immunoglobulin G (IgG)-based elimination diet among migraine patients with irritable bowel syndrome (IBS).

BACKGROUND: Food elimination has been suggested as an effective and inexpensive therapeutic strategy in patients with migraine and concomitant IBS in the past studies.

METHODS: A total of 21 patients (mean [standard deviation] age: 38.0 [11.2] years; 85.7% females) diagnosed with migraine and IBS were included in this double-blind, randomized, controlled, cross-over clinical trial composed of baseline (usual diet), first diet (elimination or provocation diets), and second diet (interchange of elimination or provocations diets) phases and 4 visits.
Results: IgG antibody tests against 270 food antigens revealed mean (standard deviation) reaction count to be 23.1 (14.1). Compared with baseline levels, elimination diet per se was associated with significant reductions in attack count (4.8 [2.1] vs 2.7 [2.0]; P < .001), maximum attack duration (2.6 [0.6] vs. 1.4 [1.1] days; P < .001), mean attack duration (1.8 [0.5] vs. 1.1 [0.8] days; P < .01), maximum attack severity (visual analog scale 8.5 [1.4] vs. visual analog scale 6.6 [3.3]; P < .001), and number of attacks with acute medication (4.0 [1.5] vs. 1.9 [1.8]; P < .001). There was a significant reduction in pain-bloating severity (1.8 [1.3] vs. 3.2 [0.8]; P < .05), pain-bloating within the last 10 days (3.2 [2.8] vs. 5.5 [3.1]; P < .05), and improvement obtained in quality of life (3.6 [1.4] vs. 2.9 [1.0]; P < .05) by the elimination diet as compared with provocation diet.

Conclusion: Our findings indicate that food elimination based on IgG antibodies in migraine patients who suffer from concomitant IBS may effectively reduce symptoms from both disorders with possible positive impact on the quality of life of the patients as well as potential savings to the health-care system.


Background: Patients with irritable bowel syndrome (IBS) often feel they have some form of dietary intolerance and frequently try exclusion diets. Tests attempting to predict food sensitivity in IBS have been disappointing, but none has utilised IgG antibodies.

Aims: To assess the therapeutic potential of dietary elimination based on the presence of IgG antibodies to food.

Patients: A total of 150 outpatients with IBS were randomised to receive, for three months, either a diet excluding all foods to which they had raised IgG antibodies (enzyme linked immunosorbant assay test) or a sham diet excluding the same number of foods but not those to which they had antibodies.

Methods: Primary outcome measures were change in IBS symptom severity and global rating scores. Non-colonic symptomatology, quality of life, and anxiety/depression were secondary outcomes. Intention to treat analysis was undertaken using a generalised linear model.

Results: After 12 weeks, the true diet resulted in a 10% greater reduction in symptom score than the sham diet (mean difference 39 (95% confidence intervals (CI) 5-72); p = 0.024) with this value increasing to 26% in fully compliant patients (difference 98 (95% CI 52-144); p<0.001). Global rating also significantly improved in the true diet group as a whole (p = 0.048, NNT = 9) and even more in compliant patients (p = 0.006, NNT = 2.5). All other outcomes showed trends favouring the true diet. Relaxing the diet led to a 24% greater deterioration in symptoms in those on the true diet (difference 52 (95% CI 18-88); p = 0.003).

Conclusion: Food elimination based on IgG antibodies may be effective in reducing IBS symptoms and is worthy of further biomedical research.

BACKGROUND: Environmental factors are thought to play an important role in the development of Crohn’s disease (CD). Immune responses against auto-antigens or food antigens may be a reason for the perpetuation of inflammation.

METHODS: In a pilot study, 79 CD patients and 20 healthy controls were examined for food immunoglobulin G (IgG). Thereafter, the clinical relevance of these food IgG antibodies was assessed in a double-blind cross-over study with 40 patients. Based on the IgG antibodies, a nutritional intervention was planned. The interferon (IFN) gamma secretion of T cells were measured. Eosinophil-derived neurotoxin was quantified in stool.

RESULTS: The pilot study resulted in a significant difference of IgG antibodies in serum between CD patients and healthy controls. In 84 and 83% of the patients, respectively, IgG antibodies against processed cheese and yeast were detected. The daily stool frequency significantly decreased by 11% during a specific diet compared with a sham diet. Abdominal pain reduced, and general well-being improved. IFN gamma secretion of T cells increased. No difference for eosinophil-derived neurotoxin in stool was detected.

CONCLUSION: A nutritional intervention based on circulating IgG antibodies against food antigens showed effects with respect to stool frequency. The mechanisms by which IgG antibodies might contribute to disease activity remain to be elucidated.


OBJECTIVE: Dietary factors have been indicated to influence the pathogenesis and nature course of inflammatory bowel diseases (IBD) with their wide variances. The aim of the study was to assess the prevalence and clinical significance of 14 serum food specific immunoglobulin G (sIgG) antibodies in patients with IBD.

METHODS: This retrospective study comprised a total of 112 patients with IBD, including 79 with Crohn’s disease (CD) and 33 with ulcerative colitis (UC). Medical records, clinical data and laboratory results were collected for analysis. Serum IgG antibodies against 14 unique food allergens were detected by semi-quantitative enzyme linked immunosorbent assay (ELISA).

RESULTS: Food sIgG antibodies were detected in 75.9% (60/79) of CD patients, 63.6% (21/33) of UC patients and 33.1% (88/266) of healthy controls (HC). IBD patients showed the significantly higher antibodies prevalence than healthy controls (CD vs. HC, P=0.000; UC vs. HC, P=0.001). However, no marked difference was observed between CD and UC groups (P=0.184). More subjects were found with sensitivity to multiple antigens (≥3) in IBD than in HC group (33.9% vs.0.8%, P=0.000). Egg was the most prevalent food allergen. There was a remarkable difference in the levels of general serum IgM (P=0.045) and IgG (P=0.041) between patients with positive and negative sIgG antibodies. Patients with multiple positive allergens (≥3) were especially found with significant higher total IgG levels compared with sIgG-negative patients (P=0.003). Age was suggested as a protective factor against the occurrence of sIgG antibodies (P=0.002).
CONCLUSION: The study demonstrates a high prevalence of serum IgG antibodies to specific food allergens in patients with IBD. sIgG antibodies may potentially indicate disease status in clinical and be utilized to guide diets for patients.


This preliminary, descriptive study after extensive clinical experience demonstrates specific IgG food RASTs done in 114 consecutive patients with strong positive histories for delayed food allergy. Elimination of the positive foods was the sole means of treatment. The symptoms leading to the test are detailed, and the method of workup is reviewed. The overall results demonstrated a 71% success rate for all symptoms achieving at least a 75% improvement level. Of particular interest was the group of patients with chronic, disabling symptoms, unresponsive to other intensive treatments. Whereas 70% obtained 75% or more improvement, 20% of these patients obtained 100% relief.


OBJECTIVE: In Irritable Bowel Syndrome, the gut-associated immune system may be up-regulated resulting in immune complex production, low-grade inflammation, loss of Class I bacteria, and translocation of inflammatory mediators and macromolecules outside of the GI lumen. Since food intolerance may be one of the reasons for this upregulation, our goal was to investigate the role of food intolerance in IBS patients.

METHODS: In this open label pilot study, we enrolled 20 patients with IBS by Rome II criteria (15 women, ages 24-81) who had failed standard medical therapies in a tertiary care GI clinic. Baseline serum IgE and IgG food and mold panels, and comprehensive stool analysis (CSA) were performed. Breath-hydrogen testing and IBS Quality-of-Life (QOL) questionnaires were obtained. Patients underwent food elimination diets based on the results of food and mold panels followed by controlled food challenge. Probiotics were also introduced. Repeat testing was performed at 6-months. We followed up with this cohort at 1 year after trial completion to assess the reported intervention and for placebo effect.

RESULTS: Baseline abnormalities were identified on serum IgG food and mold panels in 100% of the study subjects with significant improvement after food elimination and rotation diet (p < 0.05). Significant improvements were seen in stool frequency (p < 0.05), pain (p < 0.05), and IBS-QOL scores (p < 0.0001). Imbalances of beneficial flora and dysbiotic flora were identified in 100% of subjects by CSA. There was a trend to improvement of beneficial flora after treatment but no change in dysbiotic flora. The 1-year follow up demonstrated significant continued adherence to the food rotation diet (4.00 +/- 1.45), minimal symptomatic problems with IBS (4.00 +/- 1.17), and perception of control over IBS (4.15 +/- 1.23). The continued use of probiotics was considered less helpful (3.40 +/- 1.60).

CONCLUSION: These data demonstrate that identifying and appropriately addressing food sensitivity in IBS patients not previously responding to standard therapy results in a sustained clinical response and impacts on overall wellbeing and quality of life in this challenging entity.


PURPOSE: To provide evidence that elimination diet based on food-specific IgG test results is an effective, reliable and valid aid to the management of chronic medical conditions. Design/methodology/approach – A postal survey, commissioned by Allergy UK, was carried out with 5,286 subjects reporting a wide range of chronic medical conditions, who had taken a food-specific IgG enzyme-linked immunosorbant assay blood test. Questionnaires, issued three months after the results, were analysed to investigate the effect of eliminating the foods identified by the test. To check for response bias, a separate group of patients who had not responded were interviewed by telephone. The analysis and reporting of the data was carried out at the University of York. Findings – Of patients who rigorously followed the diet 75.8 per cent had a noticeable improvement in their condition. Of patients who benefited from following the recommendations 68.2 per cent felt the benefit within three weeks. Those who reported more than one condition were more likely to report noticeable improvement. 81.5 per cent of those that dieted rigorously and reported three or more co-morbidities showed noticeable improvement in their condition. For those who dieted rigorously and reported high benefit, 92.3 per cent noticed a return of symptoms on reintroduction of the offending foods.

Originality/value – These data provide evidence for the use of elimination diet based on food-specific IgG blood test results as an aid to management of the symptoms of a range of chronic medical conditions.


Irritable bowel syndrome (IBS) is one of the most common gastrointestinal disorders, having a prevalence of 12%-30% in the general population. Most patients with IBS attribute their symptoms to adverse food reactions. We review the role of diet in the pathogenesis of IBS and the importance of dietary factors in the management of these patients. The MEDLINE electronic database (1966 to Jan 2015) was searched using the following keywords: “food”, “diet”, “food allergy”, “food hypersensitivity”, “food intolerance”, “IBS”, “epidemiology”, “pathogenesis”, “pathophysiology”, “diagnosis”, “treatment”. We found 153 eligible papers; 80 were excluded because: not written in English, exclusive biochemical and experimental research, case reports, reviews, and research otherwise not relevant to our specific interest. We selected 73 papers: 43 original papers, 26 reviews and 4 letters to the editor. These papers focused on IBS pathogenesis, the association between IBS and atopy, and between IBS and food allergy, the relationship between IBS and non-celiac wheat sensitivity, the role of diet in IBS.

Pending further scientific evidence, a cautious approach is advisable, but the concept of food allergy should be included as a possible cause of IBS, and a dietary approach may have a place in the routine clinical management of IBS.
**Irritable bowel syndrome (IBS)** is one of the most common GI disorders, having a prevalence of 12%-30%.

**Most patients with IBS attribute their symptoms to adverse food reactions.**

**Studies reported that serum IgG levels are higher in patients with IBS and food allergy history, perhaps related to an inflamed or “leaky” gut.**

**Hypersensitivity reactions may play a role in causing IBS symptoms in a subset of patients.**

**Patients might have selective gut permeability to food antigens. The increase of food-specific IgG titers could be a specific reaction, rather than a non-specific response to increased gut mucosal permeability.**


**OBJECTIVE:** The causes of chronic diarrhea in children are complex. At present, food allergy is generally viewed as an important cause of this disorder, and IgG-mediated delayed allergy plays a major role in this process. This study aimed to explore the link between food specific IgG and chronic diarrhea in children, as well as the value of food antigens-specific IgG antibody detection in the management of this disorder.

**METHODS:** Eighty-two children with chronic diarrhea and 30 healthy controls were enrolled. Serum levels of specific IgG antibody to 14 kinds of food were detected using ELISA. The results were classified into four grades: Grade 0 (negative), Grade 1 (mild allergy), Grade 2 (moderate allergy) and Grade 3 (severe allergy). The patients received a diet treatment based on the results of food specific IgG antibody detection. Children with negative IgG antibody were allowed to continue their current diet. In children with Grade 1 allergy, the food responsible for the IgG antibody positive test was given only at an interval of four days. In children with Grade 2 or 3, the offending food was eliminated from the diet.

**RESULTS:** Of the 82 children with chronic diarrhea, 79 (96.2%) had increased specific IgG levels for one or more of the 14 foods tested compared to 8 (26.7%) of the controls (P <0.01). The majority of patients showed increased specific IgG levels for milk (68.3%) and egg (62.2%). A low proportion of patients (2.4%) was allergic to chicken, and no patient was allergic to pork. The symptoms were improved in 65 patients (79.3%) after 1 week to 3 months of diet treatment.

**CONCLUSION:** Food allergy is one of major causes of chronic childhood diarrhea. Food specific IgG antibody detection may assist in the dietary management of this disorder.


An increasing number of commercial tests for food allergies are marketed to consumers and healthcare practitioners with tenuous claims. The aim of this article is to provide an evidence-based review of the tests and procedures that currently are used for patients with suspected food allergy. A systematic review of the literature evaluating the validity of tests and procedures used in food
reactions was performed using conventional search engines (eg, PubMed, Ovid) as well as consumer sites (eg, Google, Bing). The National Library of Medicine Medical Subject Headings (MeSH) term food hypersensitivity was used along with food allergy testing, food sensitivity testing, food intolerance testing, and adverse food reactions. Of the results obtained, testing for immunoglobulin E (IgE)-mediated food allergy was best represented in PubMed. IgE-based testing continues to be the gold standard for suspected food allergies. Among modalities used by many conventional and alternative practitioners, 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. Mediator release testing and antigen leukocyte cellular antibody testing were only represented on consumer sites.

CONCLUSION: Further investigation into the validity and the clinical application of these tests and procedures is required. Disclosing the basis for food reactions continues to present a diagnostic challenge and testing for food allergies in the context of an appropriate clinical history is paramount to making the correct diagnosis.


BACKGROUND: A simple two-step method for the detection of specific antigen within immune complexes is described. The immune complexes are precipitated from serum by polyethylene glycol, dissociated by incubation in acid pH buffer and adsorbed onto the surface of polystyrene tubes. The antigen is detected by the binding of a radiolabelled affinity-purified specific antibody. The assay can detect the antigen within both antigen- and antibody-excess immune complexes of any immunoglobulin class and can also allow semiquantitative comparison of different samples. Immune complexes containing food protein antigens after eating have been found in the serum of both normal subjects and atopic patients; the latter group showed higher mean levels of antigen-specific immune complexes. The method can be adopted for large-scale screening of clinical samples for suspected antigens if suitable antisera are available.


OBJECTIVE: Systemic low grade inflammation may contribute to the development of obesity, insulin resistance, diabetes mellitus and atherosclerotic vascular disease. Food intolerance reflected by immunoglobulin G (IgG) antibodies may predispose to low grade inflammation and atherogenesis. We examined the relationship between IgG antibodies specific for food components, low grade inflammation and early atherosclerotic lesions in obese and normal weight juveniles. RESEARCH

METHODS AND PROCEDURES: We determined IgG antibodies directed against food antigens, C-reactive protein (CRP) and the thickness of the intima media layer (IMT) of the carotid arteries in 30 obese children and in 30 normal weight children. RESULTS: Obese juveniles showed a highly significant increase in IMT (p=0.0001), elevated CRP values (p=0.0001) and anti-food IgG antibody concentrations (p=0.0001) compared to normal weight juveniles. Anti-food IgG showed tight correlations with CRP
(p=0.001/r=0.546) and IMT (p=0.0001/r=0.513) and sustained highly significant in a multiple regression model.

DISCUSSION: We show here, that obese children have significantly higher IgG antibody values directed against food antigens than normal weight children. Anti- food IgG antibodies are tightly associated with low grade systemic inflammation and with the IMT of the common carotid arteries. These findings raise the possibility, that anti-food IgG is pathogenetically involved in the development of obesity and atherosclerosis.

CONCLUSION: Abnormal immune reactions mediated by IgG antibodies coexisted in patients with IBS. It is of great significance in treating IBS by eliminating the allergic foods according to the serum level of food-specific IgG antibodies.

“Dietary elimination therapy based on the presence of IgG antibodies to food components may be indicated. Such dietary therapy may be effective in reducing low grade inflammation and thereby preventing clinical consequences like type 2 diabetes and atherogenesis.”


OBJECTIVE: To explore the therapeutic effects on irritable bowel syndrome (IBS) by eliminating the allergic foods according to food-specific IgG antibodies and to clarify the etiopathological role and mechanism of food allergy.

METHODS: The food-specific IgG antibodies to a panel of 14 different food antigens in serum were detected with ELISA in fifty-five cases with diarrhea-dominant IBS, thirty-two with constipation-dominant IBS and eighteen normal controls. The frequency and severity index of symptoms and scores of Irritable Bowel Syndrome Quality of Life (IBS-QOL) in thirty-five cases with positive food specific IgG were observed before and after elimination of allergic foods for two months.

RESULTS: The positive rate of serum food-specific IgG antibodies was 63.6 percent in patients with diarrhea-dominant IBS and 43.8 percent in constipation-dominant IBS. Both were higher than that in normal controls. After eliminating allergic foods for four weeks according to the levels of serum food-specific IgG antibodies, the frequency of symptoms decreased from (3.79 +/- 1.58) to (1.67 +/- 0.70) per week and the severity from 3.18 +/- 1.46 to 1.52 +/- 0.67 with significant differences. After eight weeks, the frequency of symptoms decreased from (3.79 +/- 1.58) to (1.53 +/- 0.69) per week and the severity from 3.18 +/- 1.46 to 1.45 +/- 0.66, also with significant differences. After eliminating allergic foods, the overall health score and the eight dimensionality integrals of QOL except avoiding food in patients with IBS increased significantly than those before treatment. At the end of eight weeks, the symptoms relieved completely in 31.4 percent of the cases and remarkably in 34.3 percent.

CONCLUSION: Abnormal immune reactions mediated by IgG antibodies coexisted in patients with IBS. It is of great significance in treating IBS by eliminating the allergic foods according to the serum level of food-specific IgG antibodies.

BACKGROUND: Post-prandial worsening of symptoms as well as adverse reactions to one or more foods are common in the patients with functional gastrointestinal diseases, such as irritable bowel syndrome (IBS) and functional dyspepsia (FD). However, the role played by true food allergy in the pathogenesis of these diseases is still controversial and there are no well-established tests to identify food allergy in this condition.

OBJECTIVE: To investigate serum food antigen-specific IgG, IgE antibody and total IgE antibody titres in controls and patients with IBS and FD, and to correlate symptoms with the food antigen-specific IgG titres in IBS and FD patients.

METHODS: Thirty-seven IBS patients, 28 FD patients and 20 healthy controls participated in this study. Serum IgG and IgE antibody titres to 14 common foods including beef, chicken, codfish, corn, crab, eggs, mushroom, milk, pork, rice, shrimp, soybean, tomatoes and wheat were analysed by ELISA. Serum total IgE titres were also measured. Last, symptomatology was assessed in the study.

RESULTS: IBS patients had significantly higher titres of IgG antibody to crab (P=0.000), egg (P=0.000), shrimp (P=0.000), soybean (P=0.017) and wheat (P=0.004) than controls. FD patients had significantly higher titres of IgG antibody to egg (P=0.000) and soybean (P=0.017) than controls. The percentage of individuals with detectable positive food antigen-specific IgE antibodies of the three groups did not show any significant differences (P=0.971). There were no significant differences between IBS patients, FD patients and controls in the serum total IgE antibody titres (P=0.978). Lastly, no significant correlation was seen between symptom severity and serum food antigen specific IgG antibody titres both in IBS and FD patients.

CONCLUSION: Serum IgG antibody titres to some common foods increased in IBS and FD patients compared to controls. But there is no significant correlation between symptom severity and elevated serum food antigen-specific IgG antibodies in these patients.

Position Papers


