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

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Executive Summary

- FoodPrint™ and Food Detective™ products measure the physiological state of IgG antibodies to food in the body. They do not and should never be used to identify classical IgE mediated food allergies.

- There is a substantial body of published literature to indicate that the measurement of food specific IgG antibodies are a safe and clinical useful tool for the assessment of a wide variety of common conditions.

- Elimination diets based on the results of food specific IgG antibody measurements have demonstrated effectiveness in alleviating a wide variety of common conditions.

- The overwhelming majority of the negative published literature surrounding food IgG antibody measurements refers specifically to the use of IgG4 in such assessments or to the use of IgG in the assessment of food allergy. This literature therefore, should not form part of a review for the utility of food specific IgG for the investigation of food intolerance.

- **On the basis of the relevant information available, the intended use of these devices is supported by the literature.**

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).

Sampson HA, et al. (2014). Food allergy: a practice parameter update-2014: J Allergy Clin Immunol. 2014 Nov;134(5):1016-25.e43. doi: 10.1016/j.jaci.2014.05.013. Epub 2014 Aug 28

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

General Food Sensitivity

G1

Dixon, H. S. (2000). "Treatment of delayed food allergy based on specific immunoglobulin G RAST testing." Otolaryngology--head and neck surgery: official journal of American Academy of Otolaryngology-Head and Neck Surgery 123(1 Pt 1): 48-54.

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.

G2

Geoffrey Hardman, Gillian Hart, "Dietary advice based on food-specific IgG results", Nutrition & Food Science, 2007 Vol. 37 Iss: 1, pp.16 - 23

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.

G3

Mullin GE1, Swift KM, Lipski L, Turnbull LK, Rampertab SD. Testing for Food Reactions: The Good, the Bad, and the Ugly. Nutr Clin Pract April 2010 25: 192-198,

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.

G4

Prof. Nicola Volpi and Francesca Maccari. Serum IgG Responses to Food Antigens in the Italian Population Evaluated by Highly Sensitive and Specific ELISA Test. Journal of Immunoassay and Immunochemistry, 30:51-69, 2009

Abstract: Using an optimised and validated ELISA method we performed a serum test for assaying the binding capacity of serum IgG to proteins extracted from approx. 160 different foods to investigate the reactivity of specific IgG antibodies in the Italian population composed of 6,879 subjects (4,551 females and 2,328 males). 44 antigens showed an IgG response greater than 10% and only 14 aliments had an elevated reactivity greater than 20%, in particular, milk, from cow and goat, and several milk derivatives, along with egg albumin and yeasts.

The IgG response to the high reactive food antigens depending on the age of the 6880 subjects was also analysed. We demonstrated a high IgG response in a very large subject group to milk and milk derivatives, and egg albumin antigens, and we conclude that the validated ELISA test may be applied for the serum / plasma IgG antibody level determination as a useful indicator of adverse reactions to food and food hypersensitivity.

G5

Ming-Jin Zhou, Yan Zhou, Min Zhang & Wei Gao. Investigation of 14 Food Allergen-Specific IgG Antibodies in 1299 Children. International Journal of Food Properties, 19:25–30, 2016.

By analyzing 14 food allergen-specific IgG antibodies in 1299 children residing in Henan province of China, we aimed to gain a preliminary understanding of food intolerance in children living in this region. Specific IgG antibodies for 14 food allergens were semi-quantitatively detected in the sera of subjects using enzyme-linked immunosorbent assays. The total positive rate for food allergen IgG antibodies was 99.9%. Of the 14 food allergens tested, sera most frequently tested positive for specific IgG antibodies for the following five food allergens, listed from the highest positive rate to the lowest: egg, milk, soybean, cod, and crab. The total positive rate for each food allergen-specific IgG antibody showed no statistically significant gender-based differences ($p > 0.05$), nor did the total positive rate for IgG antibodies for all the types of food allergens ($p > 0.05$). The positive rates of allergen-specific IgG antibodies for milk, beef, chicken, pork, mushrooms, and eggs ($p < 0.05$) showed a statistically significant difference between the 0- to 3-year-old and 4- to 11-year-old groups. Food intolerance is prevalent in children.

Migraine

M1

Alpay, K., M. Ertas, et al. (2010). "Diet restriction in migraine, based on IgG against foods: a clinical double-blind, randomised, cross-over trial." Cephalalgia: an international journal of headache 30(7): 829-837.

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.

M2

Aydinlar, E. I., Dikmen, P. Y., Tiftikci, A., Saruc, M., Aksu, M., Gunsoy, H. G. and Tozun, N. (2013), IgG-Based Elimination Diet in Migraine Plus Irritable Bowel Syndrome. Headache: The Journal of Head and Face Pain, 53: 514–525.

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.

Irritable Bowel Syndrome (IBS)

IBS1

Atkinson, W., T. A. Sheldon, et al. (2004). "Food elimination based on IgG antibodies in irritable bowel syndrome: a randomised controlled trial." Gut 53(10): 1459-1464.

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.

IBS2

Drisko, J., B. Bischoff, et al. (2006). "Treating irritable bowel syndrome with a food elimination diet followed by food challenge and probiotics." Journal of the American College of Nutrition 25(6): 514-522.

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.

IBS3

Mansueto, Pasquale et al. "Food Allergy in Irritable Bowel Syndrome: The Case of Non-Celiac Wheat Sensitivity." World Journal of Gastroenterology: WJG 21.23 (2015): 7089–7109. Web. 19 Oct. 2016.

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.

IBS4

Kostic-Vucicevic M, Michalickova D, Dikic N, Stojmenovic T, Andjelkovic M, Nikolic I, et al. Food elimination based on immunoglobulin G antibodies improves gastrointestinal discomfort symptoms and sport performance in professional athletes. Med Sport 2017;70:480-94. DOI: 10.23736/S0025-7826.17.03102-7)

BACKGROUND: Intensive and frequent physical activity causes increase of the gastrointestinal (GI) barrier permeability leading to food intolerance. The aim was to examine the impact of 3-month

elimination diet on specific IgG antibodies level, GI discomfort intensity, body composition and sports performance of the athletes.

METHODS: 22 professional athletes participated in this longitudinal study: 12 males (mean age 25±7 years) and 10 females (mean age 25±4 years), were on a 3-month elimination diet based on the results of specific IgG food intolerance blood test. The Allergy Questionnaire for Athletes (AQUA) and Gastrointestinal Symptom Rating Scale (GSRS) questionnaires, specific IgG food intolerance blood test, basic medical examination and cardiopulmonary testing were assessed prior to and after the study.

RESULTS: AQUA scores were significantly lowered (P=0.0009). There was a trend to a significant reduction in total GSRS score (P=0.05) and a significant reduction of indigestion syndrome score (P=0.01). The level of the specific IgG antibodies was significantly decreased for all athletes and all foods they were intolerant to. Fat percent (FAT%) of the athletes decreased significantly (P=0.0008) without change in weight (P=0.06). Heart rate (HR) at the second (P=0.02) and the third (P=0.006) minute recovery phase was significantly lower. The flexibility of athletes significantly increased (P=0.001). The most important result is a significant reduction of the self-assessed indigestion syndrome.

The decrease of the IgG antibody level points out that 3-month elimination diet decreased chronic inflammation of GI tract. The diet had a significant influence on athletes' body composition and it is indirect improvement of their sports performance. Reduction of the HR at the second and the third minute recovery phase is a direct improvement of sports performance.

CONCLUSIONS: Elimination diet based on IgG food intolerance leads to a significant improvement of GI discomfort symptoms and sports performance.

IBS5

Ou-Yang, W. X., J. Y. You, et al. (2008). "[Application of food allergens specific IgG antibody detection in chronic diarrhea in children]." Zhongguo dang dai er ke za zhi = Chinese journal of contemporary pediatrics 10(1): 21-24.

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.

IBS6

Yang, C. M. and Y. Q. Li (2007). "[The therapeutic effects of eliminating allergic foods according to food-specific IgG antibodies in irritable bowel syndrome]." Zhonghua nei ke za zhi [Chinese journal of internal medicine] 46(8): 641-643.

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.

IBS7

Zuo, X. L., Y. Q. Li, et al. (2007). "Alterations of food antigen-specific serum immunoglobulins G and E antibodies in patients with irritable bowel syndrome and functional dyspepsia." Clinical and experimental allergy: journal of the British Society for Allergy and Clinical Immunology 37(6): 823-830.

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.

IBS8

Velikova TV, Altankova I, Peruhova M, Mihova A, et al. (2018). Prevalence of Specific IgG to Food Antigens in Bulgarian IBS Patients: A Preliminary Study. M J Nutr. 3(1): 017.

ABSTRACT

Since food intolerance in IBS patients may be mediated by IgG-dependent mechanisms, we aimed to investigate the prevalence of specific IgG antibodies to a panel of common food antigens in a Bulgarian cohort of IBS patients. We enrolled fifteen patients with IBS at mean age 36±10 years, diagnosed according to the Rome IV criteria. Specific IgG to food antigens in serum samples were assessed by IgG Screen Nutritional 24 ELISA. In our IBS patients we found that 40% have significant levels (> 3.51 U/ml) of specific IgG to egg white, 53,3% to cow milk, 33,3% to wheat, 20% to orange, 33,3%, to kiwi, 20% to tomato, 26,7% to garlic, 26,8% to hazelnut. Moreover, we found that 6,7 - 13,3% of IBS patients have IgG to egg white, cow milk, wheat, kiwi and hazelnut above 50 U/ml. We found also correlations of the specific IgG antibodies of some pairs of food antigens (mostly for codfish, wheat and other grains) where the correlations were assessed as moderate to strong. In conclusion, the serological determination of specific antibodies (IgG) against different food antigens may be beneficial to all individuals who are suffering from food intolerance, including patients with IBS. However, we should use these tests with caution.

Inflammatory Bowel Disease (IBD)

IBD1

Bentz S, Hausmann M, Piberger H, Kellermeier S, Paul S, Held L, Falk W, Obermeier F, Fried M, Schölmerich J, Rogler G, Clinical Relevance of IgG Antibodies against Food Antigens in Crohn's Disease: A Double-Blind Cross-Over Diet Intervention Study. Digestion 2010;81:252-264

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.

IBD2

Cai C, Shen J, Zhao D, Qiao Y, Xu A, Jin S, et al. (2014) Serological Investigation of Food Specific Immunoglobulin G Antibodies in Patients with Inflammatory Bowel Diseases. PLoS ONE 9(11): e112154.

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.

IBD3

Liu Jian, PhD, He Anqi, MM, Liu Gang, PhD, Wang Litian, MM, Xu Yanyan, MM, Wang Mengdi, MM, Liu Tong. Food Exclusion Based on IgG Antibodies Alleviates Symptoms in Ulcerative Colitis: A Prospective Study. Inflamm Bowel Dis • Volume 00, Number 00, Month 2018.

BACKGROUND: Most patients with ulcerative colitis (UC) rely predominantly on medication or disease control. Diet interventions can reduce pharmaceutical expenditures and prolong remission. We designed a prospective study to evaluate whether an immunoglobulin G (IgG)–guided exclusion diet would improve symptoms and quality of life (QoL) in patients with UC.

METHODS: The 6-month diet intervention included 97 patients with UC, who were randomly divided into an intervention group (n = 49) and a control (n = 48) group. Individual diet plans were created for the intervention group according to IgG titers; the control group ate a healthy diet as normal. Observational indices included disease activity, extraintestinal manifestations, nutritional status, and QoL. Relationships between food-specific IgG antibodies and these indices were also analysed.

RESULTS: At baseline, there were no significant differences between the groups. Food-specfic IgG antibodies were detected in 70.10% of participants. After intervention, the Mayo score was significantly lower in the intervention group than in the control group (2.41 ± 0.89 vs 3.52 ± 1.15, P < 0.05). The number of patients with extraintestinal manifestations decreased from 7 to 2 in the intervention group and from 6 to 5 in the control group. As for nutritive indices, the intervention group had higher mean body mass index and albumin than the control group (23.88 ± 3.31 vs 21.50 ± 6.24 kg/m2, respectively, P < 0.05; 48.05 ± 6.39 vs 45.72 ± 5.48 g/L, respectively, P < 0.05), whereas prealbumin and transferrin were not significantly different between the groups. QoL improved after food exclusion (P < 0.05).

CONCLUSIONS: An IgG-guided exclusion diet ameliorated UC symptoms and improved QoL. Interactions between IgG-based food intolerance and UC warrant further study.

Inflammation & Obesity

INF1

PAGANELLI, R. J. LEVINSKY & D. J. ATHERTON. Detection of specific antigen within circulating immune complexes: validation of the assay and its application to food antigen-antibody complexes formed in healthy and food-allergic subjects. Clin. exp. Immunol. (1981) 46, 44-53

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.

INF2

Wilders-Truschnig, M., H. Mangge, et al. (2008). "IgG antibodies against food antigens are correlated with inflammation and intima media thickness in obese juveniles." Experimental and clinical endocrinology & diabetes: official journal, German Society of Endocrinology [and] German Diabetes Association 116(4): 241-245.

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."

INF3

Meltem Yaman Onmus, Elif Cakirca Avcu, Ali Saklamaz. The Effect of Elimination Diet on Weight and Metabolic Parameters of Overweight or Obese Patients Who Have Food Intolerance. Journal of Food and Nutrition Research, 2016, Vol. 4, No. 1, 1-5

Abstract Obesity is caused by the chronic low-level inflammation of white adipose tissue associated with the activation of the immune system. Food intolerance (FI) is one of the probable causes of this low-level inflammation. Food intolerance test had been done to the patients who were refractory to lose weight. In this study, we tried to prove that the elimination diet, based on test results, can help with weight loss in patients. 82 patients were enrolled in the study. Their ages were between 18-65 years and had BMI ≥ 25 kg / m². The FI test was done to all of them. The patients randomized to control or FI groups. The FI group was given food intolerance elimination diet (FIED) while the patients in the control group underwent a weight loss program by supervision of a dietitian. The patient's body weight, fat weight, lean body mass, body mass index, waist/hip ratio were measured before and after the diet program of the two groups. At the same time, fasting blood sugar, lipid and A1c levels were tested. In the FI group, patients significantly lost weight 86.60±20.93 kg (BMI=31.40±4.68 kg/m2) to 77.99±14.23 kg (BMI=28.95±4.23 kg/m2) ($p<0.05$). In the control group the body weight also decreased from 89.60±17.69 kg (BKI= 33.09±4.70 kg/m2) to 88.69±18.44 kg (BKI= 32.44±5.09 kg/m2) ($p<0.05$). Body fat weight decreased from 32.22±8.18 kg to 27.00±8.27 kg in the FI group while in the control group it was decreased from 36.18±10.50 kg to 36.17±12.76 kg ($p<0.05$). Triglyceride levels of the FI group decreased significantly than the control group ($p<0.05$). There was no significant change in fasting blood glucose, A1c and cholesterol levels of two groups at the end of study ($p>0.05$). In this study, people who cannot lose weight by low-calorie diet can lose weight and fat with elimination diet according to the results of FI test. FIED is also significantly effective in triglyceride levels.

Dermatology

D1

Liu Y, Yan H, Shao F, Li QH, Cui M. Correlation between childhood eczema and specific IgG antibody level. J Biol Regul Homeost Agents. 2018 Mar-Apr;32(2):341-344.

Abstract

Eczema, a common pediatric dermatosis with unclear pathogenesis, can seriously affect the life quality of children due to its recurrence and long course. Recent study has found that food specific IgG (sIgG) might be involved in the course of eczema. To analyze the correlation between childhood eczema and sIgG and evaluate the role of avoiding taking intolerance food in the treatment of childhood eczema, this study enrolled 216 children with eczema who were admitted to the Taian Maternal and Child Health Care Hospital, Shandong, China, between August 2014 and October 2015. They were divided into an eczema group (N = 140) and an allergy group (N = 76). Eighty healthy children who were admitted to the Department of Children Healthcare in the same period were selected as a control group. Enzymelinked immuno sorbent assay (ELISA) was used to detect the serum sIgG level. The result showed that the sIgG positive rates of children in the eczema group and allergy group were 91.4% and 93.4%, respectively, and the difference had no statistical significance (P > 0.05). However, the sIgG positive rates of children in the eczema group and allergy group were significantly higher than that in the control group (P less than 0.05). Milk and eggs were the major allergy-causing food for children with sIgG positive rates higher than 70%. The sIgG test results revealed that eggs had the highest allergenicity, followed by milk, tomatoes and soybeans, and pork was not highly sensitive. Therefore, it can be concluded that sIgG positive rate of children with eczema is high, and examination of food sIgG antibody in serum is valuable in the diagnosis and treatment of childhood eczema.

D2

Jia Qi, Wei-Wei Wang, Yu-Jie Zhang, Jian Wu, Jun Wei, Li-Qing Hu, An-Quan Shang. Analysis on relationship between specific IgG antibodies of 14 food allergens and allergic skin diseases. Biomedical Research 2017; 28 (22): 9982-9985

Purpose: To analyze the relationship between the specific IgG antibodies of 14 food allergens and allergic skin diseases.

Method: 340 patients of allergic skin diseases treated in our hospital during March 2012-June 2014 are selected, including 164 males and 176 females. In addition, 30 cases of healthy people without anaphylactic reaction medical history based on the physical examination center of our hospital were selected as the control group. The food intolerance test kits (American BIOMERICA Corporation) are adopted, and the Enzyme Linked Immunosorbent Assay (ELISA) semi-quantitative detection method is applied to detect the concentrations of the antigenic IgG antibodies in 14 commonly seen foods including beef, milk, chicken and pork.

Results: The specific IgG antibodies of the 14 food allergens have different concentrations in serums of the patients; in which cod, crab, egg, milk, shrimp and soybean have relatively high contents of 15.43%,41.76%, 52.04%, 32.43%, 21.45% and 8.92%, respectively. The specific IgG antibody positive rates of the three types of skin disease patients are significantly higher than that of the control group, in which the positive rate of the urticaria group is 77.73%, with significant difference with

that of the control group (X2=173.24, P<0.05). The positive rate of the eczema group is 89.35%, which is also significantly higher than that of the control group (X2=481.52, P<0.05). The positive rate of the specific antibody of the atopic dermatitis group is 81.19%, which is also significantly higher than that of the control group (X2=274.38, P<0.05). With the growth in ages, the positive rates of the specific IgG antibodies in serums of three groups show down trends of varied extents. The chi-square test is conducted on the antibody positive rates of the patients with ages under 3 y old and that during 25-50 y old, with the result that the patients of eczema have significant difference (X2=164.23, P<0.05).

Conclusion: The serums of the allergic skin disease patients have food specific IgG antibodies, illustrating the correlation between allergic skin diseases and food intolerance. The detection on food specific IgG antibodies plays an important role in diagnosis on allergic skin diseases and prevention of food allergy.

D3

Jiesi Li, Jiawen Li, Yinfang Zheng. Detection of IL-2, IFN-γ, and serum-specific antibodies in the serum of children with atopic dermatitis. Int J Clin Exp Med 2018;11(5):5135-5140.

Objective: To investigate the expression and significance of serum interleukin-2 (IL-2), interferon-γ (IFN-γ), and serum-specific antibodies in children with atopic dermatitis (AD).

Methods: A total of 80 children with AD were selected as Group AD, and 80 infants and young children receiving physical examinations at the same period were selected as the control group. Enzyme-linked immunosorbent assay (ELISA) was used to detect immunoglobulin G (IgG) and immunoglobulin E (IgE) antibodies to allergens as well as the levels of IL-2 and IFN-γ in the serum. The levels of IgG antibodies, IgE antibodies, IL-2, and IFN-γ were compared between the two groups.

Results: The concentration of IFN-γ in the peripheral blood of the children with AD was lower than that of normal population. The difference was statistically significant (t=9.89, P=0.020). The concentration of IL-2 in the peripheral blood of the children with AD was higher than that of normal population. The difference was statistically significant (t=21.69, P<0.001). Children with AD showed relatively high positive rates of IgG antibodies to allergens: milk (43.8%), eggs (37.5%) and soybeans (10.0%), and relatively high positive rates of IgE antibodies to the milk (38.8%), eggs (41.3%) and shrimp (21.3%). The positive rates of IgE antibodies to the fish and the shrimp were obviously higher than those of IgG anti-bodies for children with AD. The differences were statistically significant (both P<0.05). The children with AD had significantly higher positive rates of IgG antibodies to the milk and the eggs than the control group (both P<0.05). They had remarkably higher positive rates of IgE antibodies to the milk, eggs, shrimp, wheat and pork than the control group (all P<0.05). There was a positive correlation between IgG and IgE (r=0.38, P=0.030), a negative correlation between IFN-γ and IL-2 (r=-0.01, P=0.040), a negative correlation between IFN-γ and IgE (r=-0.47, P=0.020) and a positive correlation between IL-2 and IgE (r=0.53, P=0.020).

Conclusion: Food allergens and inhaled allergens are important causes of AD in children. It is rapid and convenient to detect IgE and IgG antibodies and the allergens of Group AD can be detected effectively. The changes in the levels of serum IL-2 and IFN-γ play a certain role in the pathogenic process of patients with AD. Early and effective environmental control is very important for treating AD in children and preventing the occurrence of allergic diseases in the respiratory tract.

Studies using CNS Products

CNS1

Shakoor Z, Al Faifi A, Al Amro B, Al Tawil LN, Rana, Al Ohaly RY. Prevalence of IgG-mediated food intolerance among patients with allergic symptoms. Ann Saudi Med 2016; 36(6): 386-390 DOI: 10.5144/0256-4947.2016.386

BACKGROUND: Food intolerance mediated by food specific IgG antibodies has been implicated in a variety of disorders.

OBJECTIVES: To assess the prevalence of food specific IgG antibodies among patients clinically presenting with allergic symptoms lacking laboratory evidence of allergy.

DESIGN: Descriptive retrospective cross-sectional study.

SETTING: King Khalid University Hospital, Riyadh between 2010-2015.

PATIENTS AND METHODS: Patients were screened for food specific IgG antibodies. All symptomatic patients lacking laboratory evidence of allergy who underwent food specific IgG testing during the study duration were included.

MAIN OUTCOME MEASURE(S): Levels of IgG antibodies in patients with unidentified allergic symptoms.

RESULTS: We selected 71 patients with allergic symptoms lacking laboratory evidence of allergy. There were 49 female and 22 male patients mean age 38.8 (16.0) years. The majority (85.7%) had urticaria. The most frequently occurring food specific IgG antibodies were against cola nut in 80.3% of patients followed by yeast in 78.9%, wheat in 77.5%, red kidney bean in 71.8%, pea in 63.4%, corn in 62% and egg white in 62% of the patients. Compared with male patients, females harboured significantly higher food specific IgG antibodies for frequently occurring food materials, particularly against wheat (74% vs 25.5%; *P*<.0001), corn (77.3% vs 22.7%; *P*<.0001) and cola nut (71.9% vs 28.1%; *P*<.001). Patients aged less than 40 years had higher levels of food specific IgG against gliadin (*P*<.003), egg white (*P*<.03) and barley (*P*<.05) compared with older patients.

CONCLUSION: The detection of a variety of food specific IgG antibodies among patients with allergic symptoms indicates a possible link to food intolerance allergy. Females are prone to develop food intolerance more than males.

LIMITATIONS: Difficulty of comparison of results with previous studies because of lack of data. Follow-up studies could not be performed to assess the effects of elimination from the diet due to limited time allocated for this study.

CNS2

Raj Kumar, Mandeep Singh, Nitesh Gupta, Manoj Kumar, Indu Bisht, Shailendra Nath Gaur. Prevalence of food intolerance in bronchial asthma in India. Indian Journal of Allergy, Asthma and Immunology; Jul-Dec 2013, Volume 27, Issue 2

Background and Objective: Food intolerance is an adverse reaction to food in which there is no involvement of defence (immune) system. There is some evidence for the use of food-specific immunoglobulin G (IgG) levels as a guide to identify food intolerance. The current study was thus planned to study the prevalence of IgG-based food intolerance in bronchial asthma (BA) patients and healthy controls in Indian population.

Materials and Methods: A total of 65 subjects were recruited for the study comprising 50 cases of BA and 15 healthy controls. These were assessed for food intolerance using specific IgG against selected food items. The results were graded as specific IgG against the selected food item: >30 U/mL – elevated and <30 –normal as per manufacturer`s recommendation.

Results: The BA group had highest food intolerance against the vegetables, whereas in control subjects the food intolerance was highest for nuts. The prevalence of food intolerance was higher in male asthmatic patients, but in the control group females showed higher intolerance. The common food items to which food intolerance test was positive in descending order were cow milk (56%), casein (48%), tiger nut (48%), almond (46%), amaranth (46%), peanut (46%), soybean (44%), alga wakame (44%), scallop (44%), mulberry (42%) in asthmatic patients and almond (80%), cowmilk (73%), casein (66.6%), peanut (60%), cashew nut (60%), tiger nut (53.3%), carrot (53.3%), flax seed (53.3%), quino (53.3%), clan (53.3%), sunflower seed (53.3%) in control subjects.

Conclusion: The specific IgG is a test to evaluate food intolerance. The common food items to which food intolerance test was positive in descending order were cow milk (56%), casein (48%), tiger nut (48%), almond (46%), amaranth (46%), peanut (46%), soybean (44%), alga wakame (44%), scallop (44%), mulberry (42%) in asthmatic patients.

CNS3

Günay Eskici and Tülin Otbicer Acar. Two Popular Diet Models: Food Intolerance Test and Diet for Blood Group. Ind. J. Nutr. Dietet., 2014, 51, 252

This study examined the distribution consistency of the foods and the consumption of which are considered to be “forbidden or limited” by the diet for certain blood groups and of the foods considered to be “forbidden or limited” at the end of food intolerance test. The study group was composed of 102 individuals that took the food intolerance test. Foodprint®200+test, which is part of Cambridge Food Intolerance Tests, (Cambridge Nutritional Sciences-Turkey) was given to the participants, and the results were analyzed in the Cambridge Turkey laboratories. The participants identified their own blood groups. One sample ratio test was used for statistical analysis. The distribution of the participants with type A blood to the foods suggested to be “forbidden and limited” for this blood group was found not to show 80 per cent consistency at the end of the food intolerance test ($p>0.05$). Another similar inconsistency was also observed for the blood types of B, AB and O ($p>0.05$). The results of the personal food intolerance test were found not to show

minimum 80 per cent consistency with the foods included in the classification made by the diet for each blood group.

CNS4

Dean Kaličanin, Luka Brčić, Ana Barić, Sanja Zlodre, Maja Barbalić, Vesela Torlak Lovrić, Ante Punda & Vesna Boraska Perica : Evaluation of Correlations Between Food-Specific Antibodies and Clinical Aspects of Hashimoto's Thyroiditis, Journal of the American College of Nutrition 2018, DOI: 10.1080/07315724.2018.1503103

Objective: We have comprehensively evaluated an immunologic response to food antigens, mediated by immunoglobulin G (IgG) antibodies, on clinical aspects of Hashimoto's thyroiditis (HT).

Methods: IgG antibodies to 125 food antigens were measured in serum samples of 74 HT patients and 245 controls using microarray-based enzyme-linked immunosorbent assay (ELISA) test. We analyzed differences in IgG levels between two groups and evaluated correlations between foodspecific IgG levels and HT-related clinical phenotypes (thyroid hormones/antibodies, symptoms of hypothyroidism, measures of body size and blood pressure) and food consumption in HT patients.

Results: We observed increased IgG levels to 12 different food antigens in either HT cases or controls, of which plum-specific IgG antibodies were significantly higher ($p = 1.70 \times 10^{-8}$), and almond-specific IgG antibodies were significantly lower ($p=8.11 \times 10^{-5}$) in HT patients in comparison to controls, suggesting their possible roles in HT etiology or symptomatology. There was no significant correlation between any of 12 increased food-specific IgG antibodies, along with gluten-specific IgG, with clinically important phenotypes, such as thyroid hormones/antibodies or symptoms. Among other tested correlations, the most interesting is the negative correlation between coffee and tea combined IgG levels and number of symptoms, suggesting possible beneficial effect of tea and coffee on disease symptoms. We also found that food consumption is not correlated with IgG levels. Conclusions: Distribution of food-specific IgG antibodies is comparable between HT patients and controls, with the exception of plum and almond. There is no evidence that increased foodspecific IgG antibodies are associated with clinical aspects of HT. Clarification of biology behind formation of these antibodies is needed.

CNS5

Francis Coucke. Food intolerance in patients with manifest autoimmunity. Observational study. Autoimmunity Reviews 17 (2018) 1078–1080.

In the professional medical and scientific world, there is not many interest in the correlation of food intolerance and autoimmune diseases. However, there is a lot of evidence that e.g. gluten or gliadin can induce autoimmune diseases: example the interest in coeliac disease and autoimmunity. There is however a lot of information available about leaky gut and autoimmunity.

We performed an observational study in our database, where we selected 100 patients with manifest autoimmune disease with clear symptoms and autoimmune antibodies in the form of positive of more than 160 titer. These patients were compared with 25 control patients without any autoimmunity.

We could clearly find a difference in food intolerance profiles when we compared AI patients with people without any AI. Overall there is a much greater reaction to several food epitopes, which can be observed on the level of specific antibodies to the food epitopes. These igG levels for specific food antibodies are significantly higher in the patient group then in the control group. We can also see that some food epitopes provocate a very pronounced reaction, while other show no increased level of igG. Among the most reactive food epitopes are caseine, cow milk, wheat, gliadin, white of egg and rice. A variable reaction can bes een on nuts e.g.; walnuts and almonds. Almost no antibody reaction is noticed on vegetables, fish and meat products, who seem to be immunologically very neutral.

We conclude that food intolerance test is very important tool in patients with AI disease, and should be performed in each patient to tailor an individual diet program, which if properly followed, could relieve symptoms and probably stop or slow the progression of the autoimmune disease.

Also interesting for global research in AI disease is the fact that food is probably an important trigger for autoimmunity in vulnerable patients. More research on great scale and multicentre around this topic is mandatory and urgent.

Poster Presentations

institutosabin

Food –specific IgG antibodies in brazilians: a descriptive, laboratory information management system-based study.

sabin laboratório clínico

M. S. S. B. Caixeta, L.F. R. Velasco, L. F. A. Nery, S. S. S. Costa, G. B. Barra.
Laboratório Sabin, Brasília, Brazil.

Abstract:
Background:
The aim of this study was to identify the most common foods that trigger IgG immune responses in Brazilians of different age groups and describe the prevalence of this food hypersensitivity for the most common commodities available for consumption.
Methods:
We retrieved the results from our food-specific IgG antibodies test performed between December 2012 and December 2013, 279 individuals (unique) were included and 183 (65,6%) were female. The eight most common foods that trigger moderate (24-30 U/mL) or strong (>30 U/mL) IgG antibody responses were analyzed and presented by age group. The same was done with the commodities. The age groups were 1-10 (n=34), 11-20 (n=10), 21-30 (n=33), 31-40 (n=73), 41-50 (n=42), 51-60 (n=49), 61-70 (n=29), 71-80 (n=9). The food-specifics IgG assay was Genarrayt Microarray (Genesis Diagnostics), which detects total IgG against 221 foods in serum by ELISA.
Results:
The eight most commons foods that trigger IgG reaction in the patients were wheat (96,1%), cola nut (84,7%), cow's milk(75,4%), egg white (70,1%), yeast (brewer's) (64,8%), casein (59,1%), bean (57,7%) and sheep milk (57,7%) and their age-dependent relative occurrence frequency can be found in figure 2. Considering the commodities, their relative occurrence frequencies were as follows: wheat (described before), bean (describe before), maize (40%), rice (17,1%), cassava (9,3%), pigmeat (2,1%), bovine meat (0%) and poultry meat (0%). Excepting the younger, each commodity elicits a constant and specific pattern of IgG hypersensitivity over age (figure 3).
Conclusion:
We identify the most common foods that trigger moderate/strong IgG response in Brazilians and also the hypersensitive frequency for the major commodities. Some foods (Cola nut, cow's milk, egg white and brewer's yeast) showed an age dependent IgG serum levels that correlates with an expected age-dependent consumption. Conversely, the constant and specific patterns found for commodities suggest that these foods elicit specific immune response, especially when confronting the extremes (wheat versus meats).

INTRODUCTION

Previous studies have found that the levels of food-specific IgGs and IgG subclasses in blood serum were significantly higher in individuals with food hypersensitivity, and that IgG-mediated immunologic responses may play an important role in the pathogenesis of adverse food reactions. However, other studies indicate that the serum level of food-specific IgGs may also be elevated in healthy individuals, suggesting that the elevation of food-specific IgGs and IgG subclasses may merely reflect the presence of immunological tolerance to food-specific antigens, i.e., that it may only reflect a history of exposure to a certain food. Therefore, it was determined that food-specific IgGs and IgG subclasses lack diagnostic value for food allergy/intolerance (1). The aim of this study was to identify the most common foods that trigger IgG immune responses in Brazilians of different age groups and describe the prevalence of this food hypersensitivity for the most common commodities available for consumption. Also, investigate if the age-dependent IgG serum levels correlate with an expected age-dependent consumption or if the foods elicit specific immune response.

METHODS

We retrieved the results from our food-specific IgG antibodies test (Table 1 and 2) performed between December 2012 and December 2013, 279 individuals (unique) were included and 183 (65,6%) were female. The eight most common foods that trigger moderate (24-30 U/mL) or strong (>30 U/mL) IgG antibody responses were analyzed and presented by age group (Table 3 and 4). The same was done with the commodities (Table 4) (Figure 1).

Table 1: Analytical characteristics of assay.

ASSAY	MANUFACTURER	PRINCIPLE	METHOD	DETECTION
Genarrayt ™ Microarray 300+	Genesis Diagnostics Ltda.	ELISA	ELISA by Microarray	IgG against 221 foods

Table 2: Groups of Foods investigated, number of foods in each groups and some examples.

GROUPS OF FOODS	N	EXAMPLES
Dairy/Eggs	9	Cow's milk | Egg white | Casein | Sheep milk | Goat Milk
Fish/Seafood	39	Alga wakame | Clam | Alga espaguette | Scallop | Oyster
Fruits	37	Fig | Cranberry | Pineapple | Raspberry | Nectarin
Grains	15	Barley | Corn (maize) | Oat | Couscous | Spelt
Wheat	3	Wheat | Wheat bran | Durum wheat
Gluten	1	Gliadin
Herbs/spices	33	Curry (mixed spices) | Ginkgo | Mustard seed | Cinnamon | Aloe vera
Meats	16	Pork | Rabbit | Horse | Quail | Lamb
Nuts	11	Pistachio | Cashew nut | Brazil nut | Hazelnut | Almond
Vegetables	39	Bean (red kidney) | Pea | Bean (white haricot) | Amaranth | Radish
Soya	1	Soya bean
Yeast	2	Baker's | Brewer's
Others	15	Cola Nut | Agar Agar | Sunflower seed | Mushroom | Cocoa bean

Table 3: Age groups.

Age Groups	N (%)
1-10	34 (11,9)
11-20	10 (3,5)
21-30	33 (11,6)
31-40	73 (25,6)
41-50	42 (14,7)
51-60	49 (17,2)
61-70	29 (10,2)
71-80	9 (3,2)

Table 4: Commodities and the eight most foods that trigger IgG responses.

Commodities (%)	Eight most (%)
Wheat (96,1%)	Wheat (96,1%)
Bean (57,7%)	Cola Nut (84,7%)
Maize (40%)	Cow's milk (75,4%)
Rice (17,1%)	Egg white (70,1%)
Cassava (9,3%)	Yeast (brewer's) (64,8%)
Pigmeat (2,1%)	Casein (59,1%)
Poultry Meat (0)	Bean (57,7%)
Bovine Meat (0)	Sheep milk (57,7%)

(%) Percent of IgG response between the patients

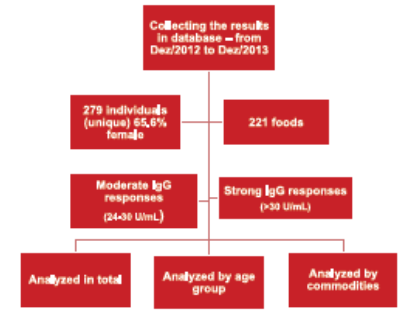

Figure 1: Methodology flowchart.

RESULTS

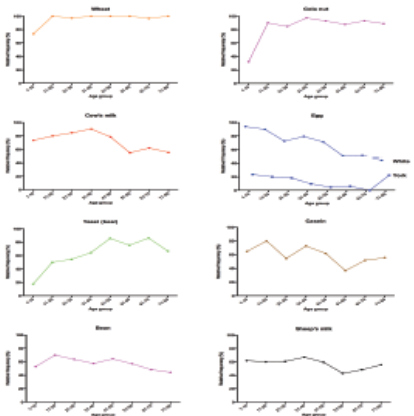

Figure 2: The eight most commons foods that trigger IgG reaction in patients and their age-dependent relative occurrence frequency.

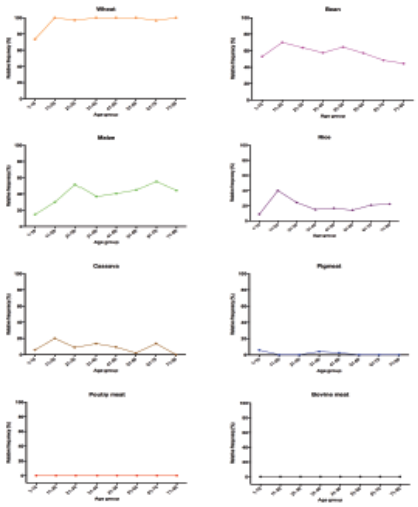

Figure 3: The eight most commons foods from the commodities and their age-dependent relative occurrence frequency.

The eight most commons foods that trigger IgG reaction in the patients were wheat (96,1%), cola nut (84,7%), cow's milk(75,4%), egg white (70,1%), yeast (brewer's) (64,8%), casein (59,1%), bean (57,7%) and sheep milk (57,7%) and their age-dependent relative occurrence frequency can be found in figure 2. Considering the commodities, their relative occurrence frequencies were as follows: wheat (described before), bean (described before), maize (40%), rice (17,1%), cassava (9,3%), pigmeat (2,1%), bovine meat (0%) and poultry meat (0%). Excepting the younger, each commodity elicits a constant and specific pattern of IgG hypersensitivity over age (figure 2). Excepting wheat and bean, the most common commodities available for consumption are not the ones that most trigger IgG reaction in the patients.

CONCLUSION

1- We identify the most common foods that trigger moderate/strong IgG response in Brazilians and also the hypersensitive frequency for the major commodities.
2 - Cola nut, cow's milk, egg white and brewer's yeast showed an age dependent IgG serum levels that correlates with an expected age-dependent consumption.
3 - Conversely, the constant and specific patterns found for commodities suggest that these foods elicit specific immune response, especially when confronting the extremes (wheat versus meats).
4 - Among the eight most common food available for consumption, only three triggered immune response in more than 40% of patients.

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Food elimination as treatment for primary headache in children

Sepideh Taheri[1], Irfaan Cader[1], Jamie Seabrook[2], Elizabeth Mazza[1], Margo De Vries[1], Craig Campbell[1]

1. Department of Paediatrics, Western University, London, Ontario, Canada
2. School of Food and Nutritional Sciences, Brescia University College at Western University, London, Ontario, Canada

Children's Hospital
London Health Sciences Centre

Western

BACKGROUND

- Chronic recurrent headache (HA) is a significant cause of morbidity in children, with a prevalence of 10% being recorded in 3-14 year olds and evidence of global increase in incidence.
- Dietary factors are considered to play a significant role in the etiology of recurrent HA in adults; however, good data to confirm this statement in the paediatric population is lacking.
- Some food triggers have direct mechanism of provoking a HA, such as caffeine, nitrites and monosodium glutamate (MSG).
- Evidence in adults demonstrates that HAs and other conditions may be secondary to an immunological mechanism mediated by immunoglobulin G (IgG) against certain foods.(1)
- Exclusion of foods based on high serum IgG levels has led to significant reduction of symptoms in adults; however, this has yet to be studied in children.

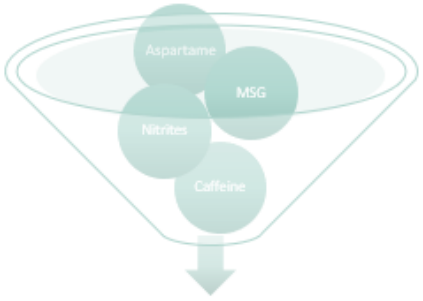

Figure 1: Common dietary HA triggers.
Previous research has demonstrated certain non-IgG mediated dietary components to be probable triggers for HAs in children and adults.

STUDY DESIGN AND METHODOLOGY

- DESIGN: Randomized, controlled, single-centre trial.
- SETTING: Outpatient tertiary paediatric HA clinic, Children's Hospital, London, Ontario.
- PARTICIPANTS: 50 children aged 7-15 referred to the HA clinic.
- EXCLUSION CRITERIA: 1) Children less than 7 years of age. 2) Secondary HA. 3) Concomitant use of complementary and alternative medication. 4) Elective surgery planned for within 24 weeks of the start of the study. 5) Diagnosis of failure-to-thrive. 6) Children with body weight plotting lower than 5th centile on a growth chart. 7) Medical conditions that in the opinion of the PI would be unsafe for trial participation. 8) Lack of follow-up or failure to comply with study procedures.
- METHODOLOGY:
- Patients are randomized to either conventional or dietary intervention group in the ratio of 1:1.
- Conventional group receive standard treatment for HA. Dietary intervention group receive targeted dietary elimination advice based on serum IgG positivity and/or non-IgG foods, based on frequency of consumption from their food diary.
- Only 1 IgG- positive food is eliminated in each 6-week visit. Handouts are given to provide alternative recipe ideas. In non-reactive patients, non-IgG foods (e.g. caffeine, MSG) are eliminated.
- Patients are followed up at 6-weekly intervals for a total of 5 study visits (24 weeks). Non-responders in each group are crossed over to the other arm of the study. Food and HA diaries are reviewed.
- IgG levels are measured at start and end of study using Food IgG Screen Kits (120 foods) provided by *Cambridge Nutritional Sciences*, and are analyzed using the ELISA technique (2,3).

INTERIM RESULTS

	Conventional Treatment	Dietary Intervention
Recruited	8 (includes 1 crossover patient)	17 (includes 10 crossover patients)
In Progress	4	4
Withdrawn	2	1
Completed	2	12

Of the 14 completed participants:

- 11 patients in diet group resolved (HA reduction >90%)
- 2 patients in diet group improved (HA reduction by 50-90%)
- 7 patients crossed study arms (6 patients from conventional to dietary and 1 from dietary to conventional due to non-response)
- 1 patient had no food triggers identified and remained in conventional group

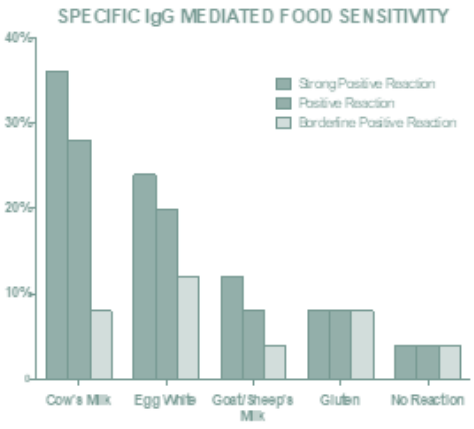

Figure 2: Common IgG mediated food sensitivities.
This figure displays centile data on the most common IgG mediated food sensitivities from all patients in the study. Patients often present with several food sensitivities.

INTERIM RESULTS

Dietary Intervention	IgG Level (%)		Δ
	Before	After	
Cow's Milk	190	106	-84%
Egg White	121	97	-25%
Goat/Sheep Milk	116	54	-62%
Gluten	103	88	-16%

Table 1: Result of dietary intervention on IgG levels..
This table displays the average relative change in IgG levels after eliminating a certain food for the period of the study. Values are represented as a percentage relative to the minimum IgG threshold required to indicate a strong positive reaction.

DISCUSSION

- Elimination of 1 or 2 foods, based on IgG positivity, has resulted in significant reduction in HA frequency and severity in children.
- This correlates well with a demonstrated reduction in serum IgG levels at the end versus beginning of the study.
- Further investigation is required to clarify the correlation between IgG-mediated food sensitivity and primary HA in children.
- We await the conclusion of this study to publish our final results.

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