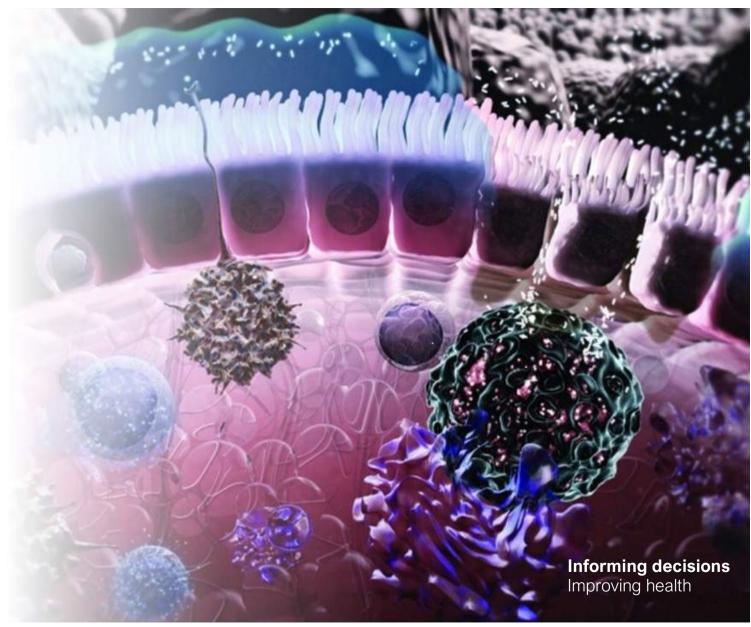


IgG Antibody Testing The Clinical Utility

Dr Nigel Abraham, PhD, FIBMS Scientific Director



Introduction

- A large body of medical literature has indicated that food sensitivity (food specific IgG antibodies) is a frequent cause of a wide range of physical and mental conditions.
- The evidence strongly suggests that identification and avoidance of reactive foods can relieve a number of common and difficult-to-treat medical problems.
- Yet the concept of food sensitivity remains controversial.

The Role of Hidden Food Allergy/Intolerance in Chronic Disease

by Alan R. Gaby, M.D.

Abstract

A large body of medical literature has indicated that hidden food allergy is a frequent cause of a wide range of physical and mental conditions. Hidden allergies can be "unmasked" by means of an elimination diet, followed by individual food challenges. Although the concept of hidden food allergy remains controversial, the evidence strongly suggests that identification and avoidance of allergenic foods can relieve a number of common and difficult-lo-treat medical problems. (Alt Med Rev 1998;3(2):90-100)

Introduction

Food allergy is well recognized in clinical medicine as a cause of acute attacks of asthma, angioedema and urticaria, and as a contributing factor in some cases of eczema and rhinitis. These types of allergic reactions are considered to be mediated by 1gE antibodies, and usually can be diagnosed by medical history and skin-prick or IgE-radioallergosorbent (RAST) tests. Another type of food reaction, often referred to as "hidden" or "masked" food allergy,

has been the subject of controversy for many years. Some practitioners have observed that hidden food allergies are a common cause of (or triggering factor for) a wide range of physical and emotional disorders. According to one estimate, as many as 60 percent of the population suffers from undetected food allergies.¹ A wide range of symptoms and disorders are reported to have a significant allergy component. See Table 1. On the other hand, many conventional physicians doubt hidden food allergy is a common problem, and some even deny altogether its existence as a clinical entity.

Skeptics emphasize the fact that many of the conditions said to be related to allergy fluctuate in severity and have a significant psychological component. Consequently, it may be difficult to distinguish between a true food reaction and a conditioned (psychogenic) response or a spontaneous exacerbation of symptoms. It also has been pointed out that food-induced symptoms should not be called allergies unless an immune-mediated mechanism can be demoustrated. While it is true many food reactions would be more appropriately labeled food intolerance, the term "allergy" will be used in this article in reference to adverse reactions to foods.

Proponents of the food allergy-disease connection argue that hidden food allergies are often overlooked because they are difficult to identify. Unlike the more obvious immediatehypersensitivity reaction that can trigger acute asthma or anaphylaxis, a hidden food reaction frequently can be delayed by many hours or even several days.

Alan R. Gaby, M.D. - Professor, Bastyr University; Past-president, American Holistic Medical Association; Contributing Medical Editor, Townsend Letter for Doctors and Patients; Contributing Editor, Alternative Medicine Roview.



Gaby AR. The role of hidden food allergy/intolerance in chronic disease. Altern Med Rev. 1998;3(2):90-100.

The controversies

- That these measurements are a normal response that simply reflect the diet of an individual.
- That such measurements cannot diagnose food intolerance.
- That the measurement of such antibodies has no role to play in the diagnosis & management of food allergy.
- It is often widely reported that food specific IgG antibody testing 'lacks sufficient validation or backed by research and is therefore not evidence-based medicine'.

3 IgG Antibody Testing – The Clinical Utility



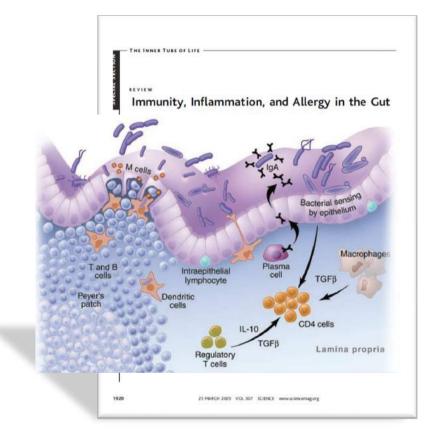


A normal immune response that simply reflect the diet of an individual?

4 IgG Antibody Testing – The Clinical Utility

Intestinal Immunity

- The gut immune system has the challenge of responding to pathogens while remaining relatively unresponsive to food antigens and the commensal microflora.
- In the developed world, this ability appears to be breaking down, with chronic inflammatory diseases of the gut commonplace in the apparent absence of overt infections.





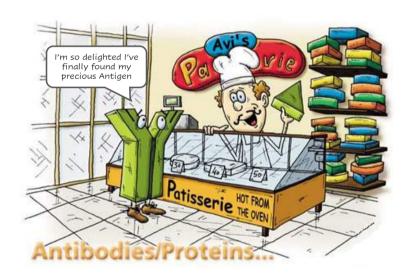
Macdonald TT, Monteleone G. Immunity, inflammation, and allergy in the gut. Science. 2005;307(5717):1920-1925. doi:10.1126/science.1106442

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What does the presence of IgG antibodies mean?

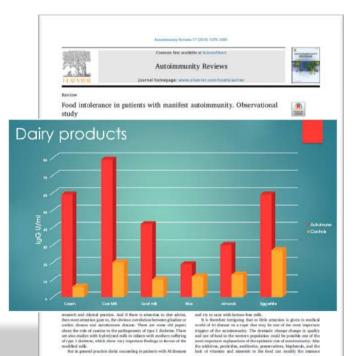


- Whilst it is a normal physiological phenomenon to produce IgG antibodies to foods, we have to remember that the presence of such antibodies in the serum constitutes an immunological defence reaction against the food.
- Tolerance is the normal state and it is not a normal reaction to develop high levels of antibodies to foods that are consumed regularly.



Prevalence

- The prevalence of migraine, irritable bowel syndrome and inflammatory bowel diseases has been continuously increasing.
- Etiological studies suggest that these diseases may be related to adverse food reactions (food sensitivity).
- Numerous studies have found that the levels of food-specific IgG's in serum are significantly higher in individuals with food sensitivity.
- IgG-mediated immunologic responses may play an important role in the pathogenesis of adverse food reactions.



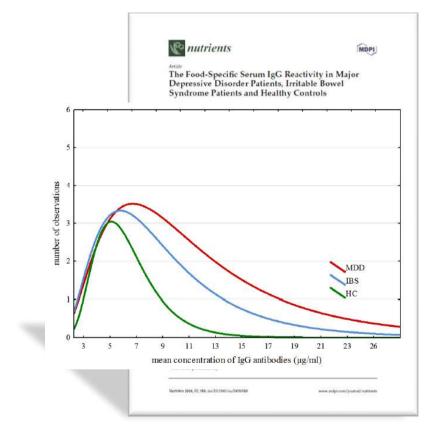


Coucke F. Food intolerance in patients with manifest autoimmunity. Observational study. Autoimmun Rev. 2018;17(11):1078-1080. doi:10.1016/j.autrev.2018.05.011

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IBS and Depression

- Figure shows specific traits of distribution of averaged results across all three groups.
- Detailed analysis of the distribution of total IgG values suggests a dissimilarity in immune responses between participants from the examined groups.





Karakula-Juchnowicz H, Gałęcka M, Rog J, et al. The Food-Specific Serum IgG Reactivity in Major Depressive Disorder Patients, Irritable Bowel Syndrome Patients and Healthy Controls. Nutrients. 2018;10(5):548. Published 2018 Apr 28. doi:10.3390/nu10050548

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That such measurements cannot diagnose food intolerance?

Classification & Terminology



9 IgG Antibody Testing – The Clinical Utility

IgG-Mediated Food Reactions / Food Specific IgG Antibodies also called:

- IgG-Mediated Food Hypersensitivity
- IgG-Mediated Allergy
- IgG Food Sensitivity
- IgG-Mediated Reactions
- IgG-Mediated Food Reactions
- IgG Food Intolerance
- IgG-Mediated Food Intolerance
- IgG-Dependent Hypersensitivity
- Food Intolerance
- Food Sensitivity
- Food-Specific IgG Antibody Testing
- 10 IgG Antibody Testing The Clinical Utility

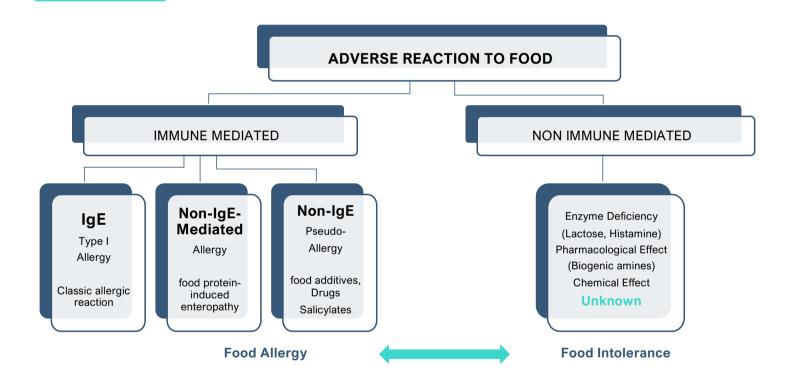
- Food Hypersensitivity
- Food IgG Antibody
- Food Sensitivity Reactions
- Chronic Food Sensitivity
- Chronic IgG-Mediated Reactions
- Type III Allergy
- Type III Hypersensitivity
- Specific IgG Antibody Testing
- Non-Immediate (Delayed) IgG Responses
- Delayed Reactions
- Classic Food Intolerance





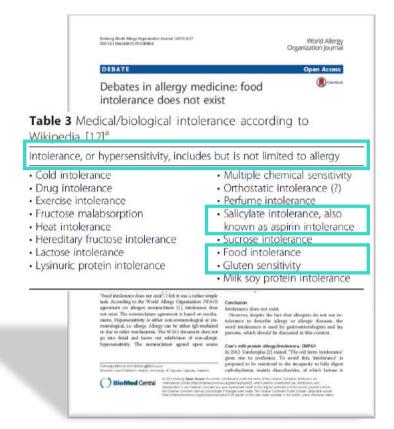
Standard Classification





Intolerance in media

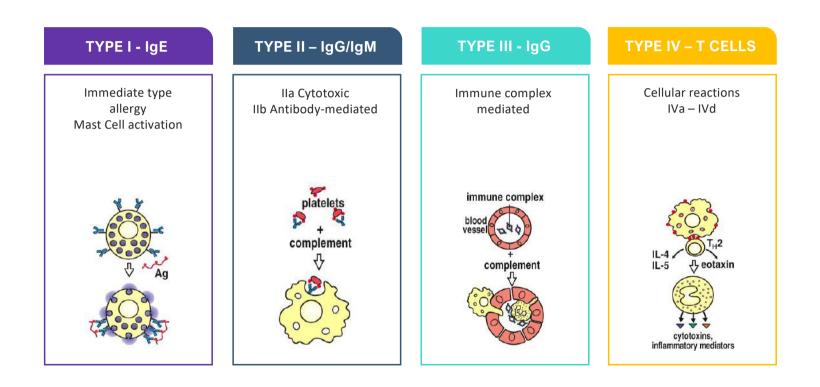
- The use of "intolerance" in lay media is often confusing.
- As an example, Wikipedia, Medical/biological intolerance.
- The introduction, "Intolerance, or hypersensitivity, includes but is not limited to allergy" is highly confusing.
- Several of the intolerances mentioned have immune mechanisms i.e. Salicylate intolerance is a form of pseudo-allergy.





Dreborg S. Debates in allergy medicine: food intolerance does not exist. World Allergy Organ J. 2015;8:37. Published 2015 Dec 14. doi:10.1186/s40413-015-0088-6

Classification of Hypersensitivity

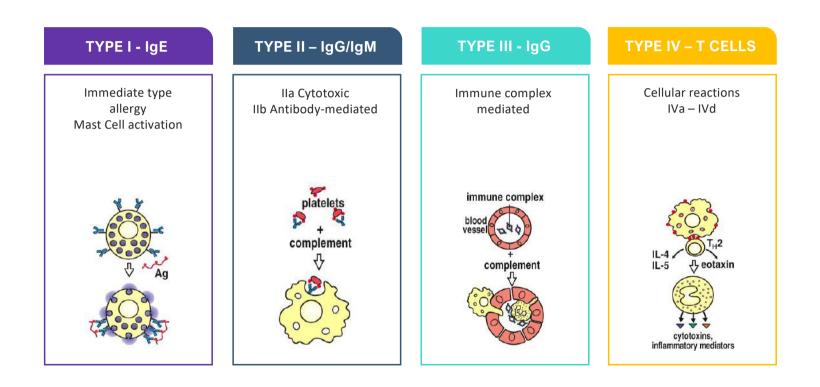




Uzzaman A, Cho SH. Chapter 28: Classification of hypersensitivity reactions. Allergy Asthma Proc. 2012;33 Suppl 1:96-99. doi:10.2500/aap.2012.33.3561

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Classification of Hypersensitivity



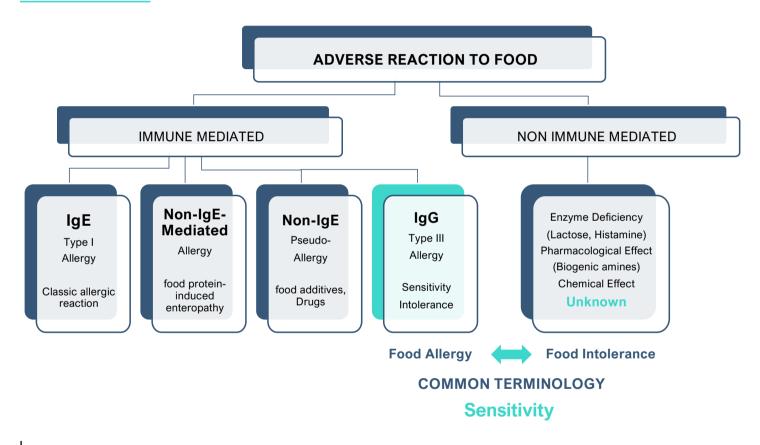
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Uzzaman A, Cho SH. Chapter 28: Classification of hypersensitivity reactions. Allergy Asthma Proc. 2012;33 Suppl 1:96-99. doi:10.2500/aap.2012.33.3561

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Standard Classification

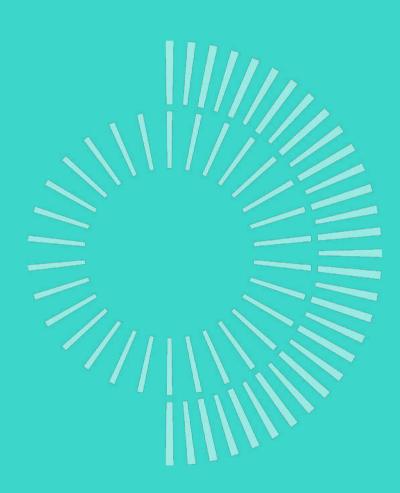






Have no role to play in the diagnosis & management of food allergy?

IgG vs IgG4



16 IgG Antibody Testing – The Clinical Utility

Antibody Classification



				Secretory component
Name	Types	%	Description	Structure
lgA	2	5-15	Found in gut, respiratory tract, urogenital tract, saliva, tears and breast milk. First line immune defense system against invading pathogens	2000 Ø
lgD	1	<1	Antigen receptor on B cells that haven't been exposed to antigens. Can produce immune response via mast cells and basophils	8 6
IgE	1	Scarce	Binds antigens and triggers histamine response from mast cells and basophils. A role in immunity to parasites but is more commonly associated with type I immediate hypersensitivity.	>>>>
lgG	4	70-85	The most abundant antibody in normal human serum. The major antibody of the secondary immune response and has the longest half-life (20-24 days). Can cross placenta to give passive immunity.	
lgM	1	5-10	Predominant antibody in the primary immune response. Used in early stages of B cell immunity before there is sufficient IgG.	×

Heavy chain domain

A J chain

17 IgG Antibody Testing – The Clinical Utility

IgG Subclass Properties



PROPERTY	lgG1	lgG2	lgG3	lgG4
Relative abundance %	60%	32%	4%	4%
Neutralisation	++	++	++	++
Activation of complement pathway	++	+	+++	
Opsonisation	+++	+	++	
Binding to macrophages	++	+	+++	++
Binding to neutrophils	+		+	

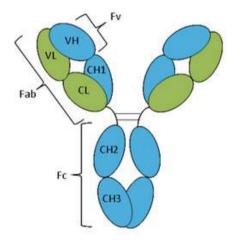
- IgG1 and IgG3 have strong pro-inflammatory properties
- IgG4 has protective, anti-inflammatory properties
- IgG4 deficiency seen in 10 to 15% of healthy patients

18 IgG Antibody Testing – The Clinical Utility

IgG4 Function



- Acts as a 'blocking agent' against the actions of IgE.
- IgG4 acts to prevent acute allergic reactions (Type I allergy) from occurring.
- No complement activation and no opsonising capacities.
- No involvement with Type III (IgG-mediated) food sensitivity.
- Invalid measurement, to detect 'delayed-onset' food sensitivity reactions.



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IgG4 as a Diagnostic Tool

- Testing of IgG4 to foods is considered irrelevant for the laboratory work-up of food allergy or intolerance.
- Testing for IgG4 against foods is not recommended as a diagnostic tool.
- However recent studies have shown that ٠ the measurement of IgG4 is of significant value in determining the likelihood of children developing peanut allergy.

Position paper	
	34 against foods is not recomme fask Force Report*
Serological tests for imm promoted for the diagnost patients believe that their diagnostic confirmation or represent a growing much linked immunesoftent as children, adolescents and 1§G4 results without corr with the lack of convinci- ling of a sensitive structure of light is transmissioned and light is transmissioned and the organism has been to the organism by the im	anophenia G4 (tgG4) aprint food a ore persistently is of food-aluced hyperentivity. Since many symptoms are related to food ingestion without of a causal relationship, tests for food-specific tgG4 at a causal relationship, tests for food-specific tgG4 at a causal relationship, tests for food-specific tgG4 and the specific transmission of the specific transmission and the transmission of the specific transmission of specific transmission of the specific transmission of the specific transmission of the specific transmission period by expression of food components, recognized an percensively, but rubates an indicator for imme- premensively. But rubates and the specific transmission of the specific transmission of the specific transmission of the specific transmission of transmission of the specific transmission of the specific transmission of transmission of the specific transmission percensively. But rubates an indicator for imme-

Allergy 2000, 62, 783-798

mological holenance, linked to the activity of regulatory T colds. In conclusion, flood-specific EqC4 does not indicate imminently found altergy or intolerance, but rather a physiological response of the immune system after exposition to food components. Therefore, resting of EqC4 to foods its considered as intelevant for the laboratory work-sp of food altergy or intolerance and should not be per-formed in case of food-rathet complaints.

0. Stapel¹, R. Asere², Jallmer-Weber², E. F. Koel⁴, bel⁸, S. Vieths⁶, J. Kleine-

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An adverse fixed reaction is a general term describing clinically abnormal responses to an ingested food that might occur secondary to nonallergic food hypersensitiv-ity (food inducennee) or allergic food hypersensitivity (food allergy). (food allergy). Frond allergy) is an immunologic reaction that involves in particular the immunophybidin E (LEE mechanism, of which anaphybias is the classic example. *Food intelerance*, however, is a gorieral term, des-ribility an unburnal physiologic response to an ingential food or food additive. Diagnosis of food insight history of an adverse reaction to frond as

altergy arms to establish a relative hash between the clinical history of an adverse reaction to food as reported by the parient and the immunological basis of this reactions. In food allergy, an accented diagross is extremely important, in particular to prevent patientis from unrecessary and even potentially health threaten-ing dists.

Mensurement of food-specific laF antibodies by in vir-Musurement of food-precific lgFanthoules by averaging or a kin sering are the readine procedures to diagnose food altergy. These diagnostic texts, however, indicate the presence of food-specific lgF as stubiols, but they do not stabilish the diagnosis of food altergy. The positive controlled Sod dualterge (1). When IgE-mediated food altergy (2) and the discussion of the specific lgF as the stubilish that dispussion of the stabilish that disapposite particular stabilish the stabilish stabilish the stabilish that disapposite stabilish the stabilish the stabilish the stabilish the stabilish the stabilish the problems, seek latter (not continuation of the proved superconducting for text reals that

for their problems, seek lattler for continuation of their personal supprison schewhere, tooking for test treatlus that are more in line with their expectations. Commorcial laboratories all over Europe are currently offering broad-scale 1gG4 testing against foods to the public, claiming that these tests represent reliable tools for the diagnosis of food allogies. This idea is probably



Stapel SO, Asero R, Ballmer-Weber BK, et al. Testing for IgG4 against foods is not recommended as a diagnostic tool: EAACI Task Force Report. Allergy. 2008;63(7):793-796. doi:10.1111/j.1398-9995.2008.01705.x

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IgG4 & Peanut Allergy

 Among infants with high-risk atopic disease, sustained peanut consumption beginning in the first 11 months of life, as compared with peanut avoidance, resulted in a 86% reduction in peanut allergy at 60 months of age.

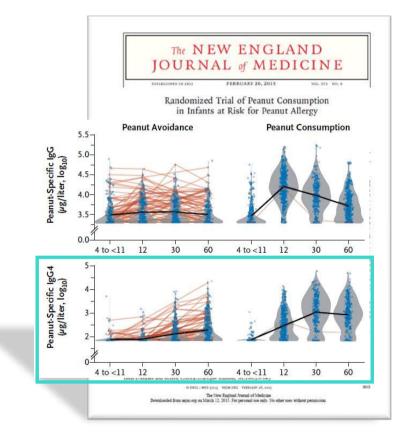




Du Toit G, Roberts G, Sayre PH, et al. Randomized trial of peanut consumption in infants at risk for peanut allergy [published correction appears in N Engl J Med. 2016 Jul 28;375(4):398]. N Engl J Med. 2015;372(9):803-813. doi:10.1056/NEJMoa1414850

IgG4 & Peanut Allergy

- In the avoidance group, unless peanut-specific IgE levels were very high, elevated IgG4 levels were associated with the absence of an allergic reaction to peanuts.
- These observations indicate that IgG4 is associated with a protective role against the development of allergy.



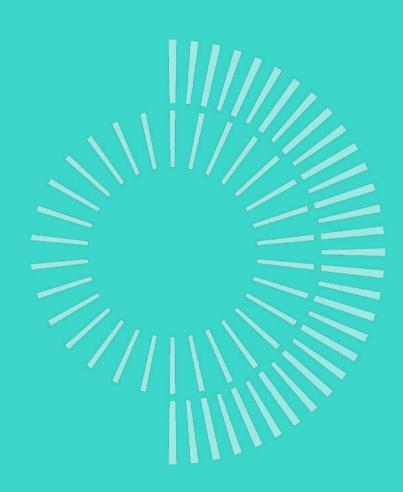


Du Toit G, Roberts G, Sayre PH, et al. Randomized trial of peanut consumption in infants at risk for peanut allergy [published correction appears in N Engl J Med. 2016 Jul 28;375(4):398]. N Engl J Med. 2015;372(9):803-813. doi:10.1056/NEJMoa1414850

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Outdated and inaccurate statements?



23 IgG Antibody Testing – The Clinical Utility

- A new review aims to help physicians diagnose and manage food allergies in children and adults. The article, published in CMAJ (Canadian Medical Association Journal 2016) looks at recent evidence from guidelines, randomized controlled trials and other research.
- "Food-specific [IgG] testing is being increasingly used to identify food "sensitivities," they state. "This testing has not been validated nor supported by research."

"There is no validity': Unproven blood tests for food sensitivity widely offered in Canada

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More than 2 dozen health groups have warned about misuse, misinterpretation of IgG tests for food intolerance

Charlsie Agro, Tyana Grundig - CBC News - Posted: Nov 02, 2018 4:00 AM ET | Last Updated: November 2, 2018



Two of Canada's biggest labs, Dynacare and LifeLabs, promote and offer something known as IgG food tests at their labs, marketed as a way to test for food sensitivities. (John Lesavage/CBC)



Abrams EM, Sicherer SH. Diagnosis and management of food allergy. CMAJ. 2016;188(15):1087-1093. doi:10.1503/cmaj.160124

- In this review, we focus on immunoglobulin E (IgE)-mediated food allergy and address key issues in its diagnosis and management.
- The Canadian Society of Allergy and Clinical Immunology had previously released a position statement discouraging the use of IgG testing to identify an adverse food reaction, echoing a similar sentiment expressed by the American Academy of Allergy, Asthma and Immunology

СМАЈ	K	EVIEW
Diagnosis and manager	ment of food allergy	
Elissa M. Abrams MD, Scott H. Sicherer MD		
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After identifying common issues facing primary cars providers in the diaposis and near-agreement of food allerings, we used record Canadam. American and international prostice patienters review, togetamental with a search for systematic reviews for supporting internations. Additional direct points and search for systematic reviews for supporting internations. Additional direct points and search for based on reviews, where retricted on search to	comment. ⁴ Although respiratory symptoms are KEV POINTS Produ altergy has a characteristic and reproductly predictive value and offens iterative for the symptometry. The only tile scaring tentement for food-induced groupptrize. Egg altergy in rol a contraindication to enhume	t has a low positive significant sensitization. Lanaphylaxis is
Explicit-language articles. Where possible, we selected the must recent articles and the articles with the most robust level of evidence. We reviewed more than 100 citations, of which 54 are included in this review.	 ogg angenetisen, Allergies to milk, egg, sig and wheat will ready most instance; allergies to jeanuts, free nuts an persist. 	e during childhood in



Abrams EM, Sicherer SH. Diagnosis and management of food allergy. CMAJ. 2016;188(15):1087-1093. doi:10.1503/cmaj.160124

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4.2.2.9. Nonstandardized and unproven procedures.

Guideline 12: The EP recommends not using any of the following nonstandardized tests for the routine evaluation of IgE-mediated FA:

- Basophil histamine release/activation^{138,139}
- Lymphocyte stimulation^{140,141}
- Facial thermography¹⁴²
 Gastric juice analysis¹⁴³
- Endoscopic allergen provocation¹⁴⁴⁻¹⁴⁶
- Hair analysis
- Applied kinesiology
- Provocation neutralization
- Allergen-specific IgG₄
- Cytotoxicity assays
- Electrodermal test (Vega)
- Mediator release assay (LEAP diet)

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Guidelines for the Diagnosis and Mana Allergy in the United States: Report of Expert Panel	

Find allergy is an important public health problem that affects children and adults and may be increasing in provinces. Despits the risk of a source abrain reactions and a cone death, there is no current treatment for field allergy: the disease cur-why be managed by allergan evolutions or treatment of symptoms. The dispussion and assumptions of adults of allergy abrain regions. The dispussion and assumptions of the distance to symptom. The dispussion and assumptions of the distance of symptoms. The dispussion and assumptions of the distance because publics. Frequently confine annulating the distance of anisothed built among the public that fields allergy providence in higher than it truly is. In response to thus concerns, the anisothed built of the distance of the distance fractions. estitute of Allergy and I with 34 professional organizations, federal agencies, and pa advocacy groups, led the development of clinical guideline the dim nis and management of food allergy. These Guidalin are intended for use by a wide variety of health care demicraty, including family practice physicians, clinic oreansate, including family practice physicians, edimate ecidists, and more practicianses. The Goldkinss include a menusa definition for food allergy, discuss consorbid editions often associated with food allergy, and focus on both K-mediated and son-IgE-mediated reactions to food. Topics rga-metatont and non-glg-modiated reactions to food. Topica addressed include the spidemiology, natural history, diagonis, and management of food allerge, as well as the management of savers symptoms and anaphytanis. These Guidelines periodic A2 coursize diside recommendations and additioning quickness on points of cerrent controversy in patient management. They also identify again in the current solution. power management. The, through future research. (J Allergy Clin Intronast 20(0;126:S1-885.) Ker words: Food, allerer, anapirolanti, diseast, diseast

SECTION 1. INTRODUCTION

1.1. Overview voot allergy (19A) is an important public health problem that rets toldys and children and may be increasing in provalence. ere allergie re for FA: the di-

nal concerns relate to the differences in the diagnosi ment of FA in different clinical practice settings rse concerns, the National Institute of Allergy and iscoses (NIAED), part of the National Institutes of RR: Robelley and SAFE Sock support, Allergen identification and over Follow up with specialty care, Epinepianis for ting with more than 30 professional organization ensergendes dgfl. Allergez-specific lgfl SPT: Note prick ust WAO: World Allergy Organiz

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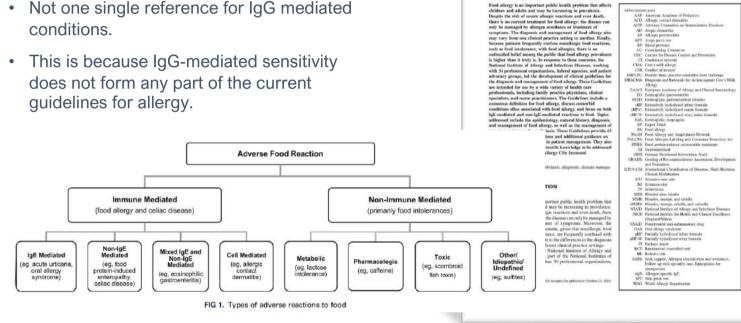
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C00	Conflict of integrat
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EAACT	European Academy of Allingy and Christal Immunology
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FAAN	Food Allergy and Anapirelanis Network
	Pool Allergra Labrilag and Consumer Protection Act
FP15S	Food protein-induced enterocolitis syndrome
62	Garmeintestizal
CENT	German Notettional Intervention Study
	Grading of Recommendations Assessment, Development
	and Finalization
ICD-9-CM	International Classification of Diseason, Nucl. Revision.
	Chrokesi Medafication
3000	Intensive-cost and
Bd.	3creanswaler
	litterven.eus
- MD1	Motouri-dawn islialer
MMR	Measles, moreps, and ratella
MMRV.	Measles, neurops, subella, and sortcolla.
	National Institute of Allogy and Infectious Diseases
NUE	Netional Institute for Health and Clinical Excellence
	(England/Widom)
	Nonisteroialal anti-miliananatory strug
045	Onal allengy syndrome.

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NIAID-Sponsored Expert Panel, Bovce JA Assa'ad A, et al. Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. J Allergy Clin Immunol. 2010;126(6 Suppl):S1-S58. doi:10.1016/j.jaci.2010.10.007

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- 347 papers cited •
- Not one single reference for IgG mediated conditions.
- This is because IgG-mediated sensitivity ٠ does not form any part of the current guidelines for allergy.



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Expert Panel

Field allergy is an important public health problem that affects children and adults and may be increasing in provinces. Dogsith the risk of scores abeying reactions and even death, there is no corrent transmission for final allergy: the disease cru services. The health is a score of the disease of the image vary from one clinical practice setting to another. Finally, became publics through score of the adult of the disease in a score of the score of the disease of the disease in adult of the score of the score of the disease of the adult of the score of the score of the disease of the adult of the score of the score of the disease of the adult of the score of the score of the score of the score of the inhight of the score of the score of the score of the inhight of the score of the score of the score of the score of the inhight of the score of the score of the score of the score of the inhight of the score of the score of the score of the score of the inhight of the score of the score of the score of the score of the inhight of the score of the score of the score of the score of the inhight of the score o

with 34 perfersional organizations, federal agencies, and patient advocacy groups, left the development of clinical guidelines for the diagonia and management of food allergy. These Guidelines

are intended for use by a wide variety of bealth care professionals, including family practice physicians, clinical

Guidelines for the Diagnosis and Management of Food

Allergy in the United States: Report of the NIAID-Sponsored



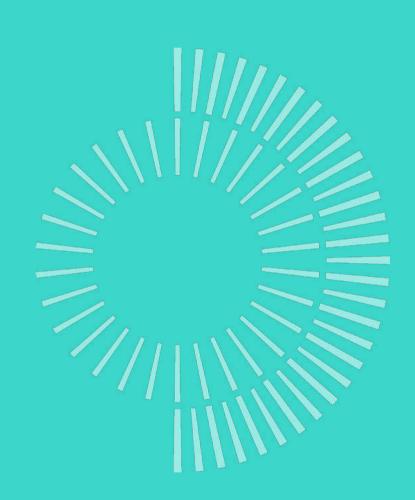
NIAID-Sponsored Expert Panel, Bovce JA. Assa'ad A, et al. Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. J Allergy Clin Immunol. 2010;126(6 Suppl):S1-S58. doi:10.1016/j.jaci.2010.10.007

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'lacks sufficient validation or backed by research and is therefore not evidence-based medicine'?



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Research Papers



- General IgG-mediated reactions
- Irritable Bowel Syndrome (IBS)
- Migraine
- Inflammation, obesity & arthritis
- Asthma / respiratory diseases
- IBD: Crohn's disease, Ulcerative Colitis
- Neurological
 - · Schizophrenia
 - Depression
 - Autism

29	IgG Antibody Testing – The Clinical Utility
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IBS: A Role For IgG

- 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.
- Review of publications (1966 to 2015)





Mansueto P, D'Alcamo A, Seidita A, Carroccio A. Food allergy in irritable bowel syndrome: The case of non-celiac wheat sensitivity. World J Gastroenterol. 2015;21(23):7089-7109. doi:10.3748/wjg.v21.i23.7089

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IBS: A Role For IgG

Reported that:

- Serum IgG levels are higher in patients with IBS related to an inflamed or "leaky" gut.
- Selective gut permeability to food allergens.
- The increase of food-specific IgG could be a specific reaction, rather than a nonspecific response to increased gut mucosal permeability.

Pending further scientific evidence the concept of food sensitivity should be included as a possible cause of IBS, and a dietary approach may have a place in the routine clinical management of IBS





Mansueto P, D'Alcamo A, Seidita A, Carroccio A. Food allergy in irritable bowel syndrome: The case of non-celiac wheat sensitivity. World J Gastroenterol. 2015;21(23):7089-7109. doi:10.3748/wjg.v21.i23.7089

Informing decisions Improving health

Irritable Bowel Syndrome -ACG Guidelines

- We recommend a limited trial of a low fermentable oligosaccharides, disaccharides, monosaccharides, polyols (FODMAP) diet in patients with IBS to improve global symptoms.
- Multiple tests are marketed to diagnose food sensitivities; however, none have been validated, and most have not been subjected to rigorous, blinded trials.
- Serum IgG panels have not been validated and cannot be recommended at present.

ACG Clinical Guideline: Mar	nagement of Irritable
Bowel Syndrome	0
Brian E. Lacy, PhD, MD, FACG ¹ , Mark Pimentel, MD, FACG ¹ , Dane Laurie A. Keefer, PhD ⁶ , Mille D. Long, MDMPH, FACG (GRADE Me	
following: We suggest that a positive diagnostic strategy as con- time to initiating appropriate therapy. We suggest that seeks with IBS and diamhea symptomes. We suggest that teach symptoms to rule out inflammatory bawel disease. We recom- disacchardies, monotacchardes, polyois (PODMAP) detrin p the use of chloridie channel activators and guarylate cyclase	atients with IBS to improve global symptoms. We recommend
	ea symptoms. We suggest that gut directed psychotherapy be ad information regarding diagnostic strategies, specific drugs, r.
used to treat global IBS symptoms. Additional statements ar doses, and duration of therapy can be found in the guideline	he symptoms. We suggest thatgut directed psychotherapy be d information regarding diagnostic strategies, specific drugs, L.

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Lacy BE, Pimentel M, Brenner DM, et al. ACG Clinical Guideline: Management of Irritable Bowel Syndrome. Am J Gastroenterol. 2021;116(1):17-44. doi:10.14309/ajg.000000000001036

Food Specific IgG Vs FODMAP

- The aim of the study was to compare the effectiveness of three different diet plans in treating patients with mixed IBS:
- G1-FM-low-FODMAP diet
- G2-IP-IgG-based elimination-rotation-diet
- G3-K Control group, classic diet recommended by an attending gastroenterologist
- Significant differences in reduction of IBS symptoms were found between groups

More Effective than FODMAP Diet and Control Diet in the Treatment of Women with Mixed IBS-Results from an Open Label Study Lucyna Ostrowska 📆 Diana Wasiluk 💷 🔍 Camille E J. Lieners ¹, Mizosława Gałęcka ², Anna Bartsicka and Dag Tweiter Dynamical and Kawata and Kiman Andra, Mahata Ukiwenty et Balyotak, ut Musika Li R. Milhi Handah, Nacha Interna astronomical and anti-landhar on Marsencheng at Stellak 20, 40 DF Jonne, Diriont, Gherentyk Jr. S. 11, 1, anglochalilingti and materialogi at M. Cara and henrickalinghene metericaling (4), 63 Leil Mohata Labaratary, Elin Endertervi H. 107 Sandrik, Norwey, Hillefold an Compregention: Analysis analabilitativa data (2), 42 - 14807 2023 2014 tract. Initiable bound strateoms (DBS) is a chemic d narbod bowel emptying, and changes in stool consistency. We compared the effectiveness of three different distary incoment plans (G1-PM-low PCEMAP dist, C2-PFgG based eliminature-mattee dist, and as correal group, the C3-Se control dist recommended by an adminiling gattreentendiget) in Check for speakers Chattan: Onrovita, L. Masiluk, II. Loren, C.F.J. Galacka, M. Battaba, A. Tustan, D. Igg/food nationaly masting matients discovered with mixed initiable bound similaring. A total of seconds three formal thering patients diagnosed with mixed minutes environments. A time of sectory time annue patients diagnosed with a mixed form of initialite bowel syndrome. (IRS-M) were envilled in the study. The diet of each patient in Group 1 (G1-M) and 2 (G2-M) was determined individually during a monting with a dietitian. Patients from Group 3 (G3-K) received matrition advice from a Coldey Elementers Reason Dark Via More Effective than FCOMAP nastroentoelogist. Semilicant differences in the reduction of IBS semetants were found betw User and Commit Dati in the gastrosteristopist. Significant differences in the reduction of BS symptoms were hund between the groups. IBS symptoms as well as consorbid symptoms significantly improved or disappeared completely is the C2-IP groups (disoptimic abdomia) paint $\rho = 0.001$; abdomiant pain after a meal, p < 0.003; abdomiant pain sharing delecation, $\rho = 0.003$, while in the C1-FM group, some of the IBS ment of Piceson with Mixed and the same farmer of du 1 Clay Ador 2022 IV 412 symptoms significantly improved (macus in ecod p=0.00; biosting, p<0.001. In group GAK no significant improvement was seen. Based on the results of this open-label study, it was concluded that various dietary interventions in the treatment of BIS-M patients do not uniformly affect the course and outcomes of disease management. Rotation diets haved on IgCl show significantly beth results compared to other diets. Restort Dillow 201 Keywords: unitable bowel syndrome (IIB); IgG lood hypersenuitivity; elimination-rotation die Fublished: 20 September 2021 low FODMAP dist classic dictary recommendation: colomatectia tills lamit their space balls 1. Introduction Introduction
 Introduction for the series of the . segregate 2 101 ty for earlies that adequate dirtary modifications can recover active influencing the classical symptoms that adequate dirtary modifications is an important lactor influencing the classical symptoms admittent under two and of REIS-1. This view is equiprotect by prosticulations that the classical symptoms admittent due classical classical symptoms centring after food intake. Patients with BS often eliminate some introduces CR hysteric lassical symptoms centring after food intake. Patients with BS often eliminate some introduces CR hysteric lassical symptoms centring after food intake. The symbol or manewus studies indicate thus FOOMAP environments equiversity in the dist cause or intensity symptoms of IBS and that in centrast, 4 law FOOMAP dist

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Ostrowska L, Wasiluk D, Lieners CFJ, Gałęcka M, Bartnicka A, Tveiten D. Igg Food Antibody Guided Elimination-Rotation Diet Was More Effective than FODMAP Diet and Control Diet in the Treatment of Women with Mixed IBS-Results from an Open Label Study. J Clin Med. 2021;10(19):4317.

Published 2021 Sep 23. doi:10.3390/jcm10194317

Informing decisions Improving health

Food Specific IgG Vs FODMAP

- All IBS symptoms as well as comorbid symptoms like headache, skin conditions, constant tiredness/weakness significantly improved or disappeared completely in the G2-IP group (p<0.008).
- While in G1-FM group only some IBS symptoms like bloating, gastric fullness significantly improved.
- In group G3-K no significant improvement was seen.
- **Conclusion:** The most effective diet in the treatment of patients with mixed IBS was the eliminationrotation diet based on IgG-dependent food hypersensitivity test.

Isunal of Clinical Medicine

Igg Food Antibody Guided Elimination-Rotation Diet Was More Effective than FODMAP Diet and Control Diet in the Treatment of Women with Mixed IBS—Results from an Open Label Study

MDPI

Lucyna Ostrowska 100, Diana Wasiluk 1.40, Camille F. J. Lieners ², Mizosława Gałęcka ², Anna Bartsicka ²

Table 3. Frequency of IBS symptoms in studied patients before and after dietary treatment.

			G1-FM			G2-IP		G3-K		
Symptoms			2nd examination	р	1 st examination	2 ^{od} examination	Р	1 st examination	2nd examination	Р
Idiopathic	N	15	11		16	2	horomed	16	14	Samore
abdominal pain	%	57.7	42.3	0.125	76.2	9.5	0.000	61.5	53.8	0.500
Abdominal	N	11	6		14	2	0.000	14	12	0.625
pain after a meal	%	42.3	23.1	0.063	66.7	9.5		53.8	46.2	
Abdominal	N	5	2		9	1	0.008	6	6	1.000
pain during defecation	%	19.2	7.7	0.250	42.9	4.8		23.1	23.1	
Sensation of	N	13	10	10000	13	2	i contra de	14	15	England -
incomplete defecation	%	50.0	38.5	0.250	61.9	9.5	0.001	53.8	57.7	1.00
Manual in stand	N	8	2	0.031	δ	0		5	6	1.000
Mucus in stool	%	30.8	7.7	0.031	28.6	0.0		19.2	23.1	
Blood in stool	N	3	0		2	0	- 140 I	2	2	1.000
	%	11.5	0.0		9.5	0.0	1 8	7.7	7.7	1.00
Difficulty to	N	11	7	0.219	14	4		19	17	
defecate (constipations)	%	42.3	26.9		66.7	19.0	0.002	73.1	65.4	0.50
Bloating	N	22	7	0.000	19	2	0.000	24	22	0.500
Bloating	%	84.6	26.9	0.000	90.5	9.5		92.3	84.6	
Gurgling	N	17	4	0.000	18	2	0.000	21	19	0.500
sensation	%	65.4	15.4	0.000	85.7	9.5		80.8	73.1	
Gastric	N	15	3	0.000	19	2		22	19	0.250
fullness	%	57.7	11.5	0.000	90.5	9.5	0.000	84.6	73.1	1 0.25



Gałęcka M, Bartnicka A, Tveiten D. Igg Food Antibody Guided Elimination-Rotation Diet Was More Effective than FODMAP Diet and Control Diet in the Treatment of Women with Mixed IBS-Results from an Open Label Study. J Clin Med. 2021;10(19):4317. Published 2021 Sep 23.

IgG vs FODMAP Diet

- This study shows that a personalised dietary approach is more effective in treating IBS-M than generalised diet recommendations.
- Only the IgG elimination-rotation diet could demonstrate significant improvements in all of the monitored IBS-M symptoms as well as extra-intestinal symptoms.
- One possible strategy could be to start with the elimination-rotation diet, as it was proven to be the more effective diet in this open study, and in cases of persistent symptoms, it could be combined with a low-FODMAP diet.





Ostrowska L, Wasiluk D, Lieners CFJ, Gałęcka M, Bartnicka A, Tveiten D. Igg Food Antibody Guided Elimination-Rotation Diet Was More Effective than FODMAP Diet and Control Diet in the Treatment of Women with Mixed IBS-Results from an Open Label Study. J Clin Med. 2021;10(19):4317. Published 2021 Sep 23. doi:10.3390/icm10194317

IgG & Migraine - Review

- Utilising IgG food sensitivity testing to • create customisable dietary recommendations for patients may allow healthcare providers to treat migraine headaches without the use of medications as cost-effective alternative.
- While elimination diets without the use of IgG serum testing may be utilised by practitioners, the time-consuming nature of this process may prove challenging for both patients and practitioners.

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101 TOPICS IN PAIN AND HEADACHE (N ROSEN, SECTION E	DITOR
he Clinical Use of IgG Food Sensitivity leadache Patients: a Literature Review	
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bished online: 27 August 2019 Springer Science-Busines Media, LLC, pet. of Springer Nature 2019	
subcless: some Findings [gG food sensitivities have been linked to s indrances an encograred within the clinical medicine com- ulturying because symptoms are usually dehyed hours to reserve proor indicate that food such is chicolatat, dhese is adaletes. mensity The pathophysiology of nigmine boalacles is not- metisty totating to determine food sensitivities and nucleance challeters.	hip botwon (gG load sensitivities and their relation to negatine ations symptoms and deserters. While field sensitivities and munity, disgraving these sensitivities and indetences can be days and may not occur after every exponent to the allegan- cons's milk, eggs, and real wise may be tliggers for migraine well indetenced. Some existence supports the use of [gG: food as [gG] code and the postgravity of the transfer of the gravity relif indetenced. Some existence supports the use of [gG: food an [gG] code and the postgravity of the transfer of the gravity relif indetenced some sensitivity of the sensitivity rates may allow healthcare providers to treat migmine headsche
rywords. Food sensitivities - LgG - Migraine - Hendaches	
troduction ignine hadaches are debilitating and affect roughly 15% of edults in the USA and have socioeconomic and personal splications [1] It has been reported that women are affected instrume headoches, at a net needy three times these of	syndrome, and inflammatory bowel disease [5–]. Food sensi- tivities are believed to be immunological mediated reactions to fixed that we impost [6–, 7]. These hidden sensitivities and intelemences are often delayed and may take hours to days to manified [5–, 8]. Complexing this time component is the fact that these sensitivities and indepense more not show score

men [2] According to Mitchell et al. migraine headaches after comunities the field in meetion [5w] mm [2]. According to Mittell et al., magname bankabes after consuming the boot in question [29]. The format of some (2]. The some transmission of food allergies or sensitivities and not even know it [5+]. Food sensitivities and intolerances are well recognized

prove beneficial for better treatment outcomes [6+]. Evidence suggests that IgG-based food sensitivities and intelerances are within clinical medicine and have been linked to various symptom and disorder including utriaria, angicedarus, ee erems, nignines, portisis, fistiges, clinitis, irritatis bound sources and angi be inggread by the con-eners, nignines, portisis, fistiges, clinitis, irritatis bound and the second sources and the second fruits, and red wine [10-12].

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Department of Hindib and Movement Science, Graceland University, University PL, Lancon, 5A 30140, USA

tarticle is part of the Topical Collection on Hisr Topics in Pain and Discussion

In clinical practice, it can often be difficult to identify the underlying food intolenances inquestion and symptome may vary patient-to-patient [5**]. The exact pathophysiology

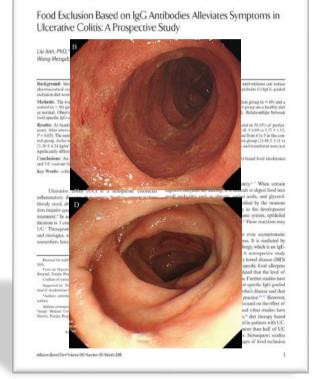
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Geiselman JF. The Clinical Use of IgG Food Sensitivity Testing with Migraine Headache Patients: a Literature Review. Curr Pain Headache Rep. 2019:23(11):79. Published 2019 Aug 27. doi:10.1007/s11916-019-0819-

Food IgG & Ulcerative Colitis

- Most patients with ulcerative colitis (UC) rely predominantly on medication for disease control.
- Diet interventions can reduce pharmaceutical expenditures and prolong remission.
- Typical endoscopic findings.
- Food exclusion group before intervention.
- Food exclusion group after intervention.



FUTURE DIRECTIONS



Jian L, Anqi H, Gang L, et al. Food Exclusion Based on IgG Antibodies Alleviates Symptoms in Ulcerative Colitis: A Prospective Study. Inflamm Bowel Dis. 2018;24(9):1918-1925. doi:10.1093/ibd/izy110

Food IgG & Ulcerative Colitis

- In conclusion, sticking to an IgG-based exclusion diet effectively improved symptoms and health-related QoL in patients with UC.
- In the future, dietary interventions will play an increasingly important role in UC management, acting as a viable option to reduce symptoms, shorten the course of disease, and speed up recovery.
- An IgG-based exclusion diet may ultimately reduce the economic burden of this disease



FUTURE DIRECTIONS

Food Exclusion Based on IgG Antibodies Alleviates Symptoms in Ulcerative Colitis: A Prospective Study

Liu Jian, PhD,* He Angi, MM,* Liu Gang, PhD, Wang Litian, MM, Xu Yanyan, MM, Wang Mengdi, MM, and Liu Tong, PhD

Background: Most patients with identify collin (UC) rely predominantly on medication for disease contrid. Deit interventions can red-futurmization expenditums and pushor priminants. We designed a prospective study to exhaust whether an itermanylabelin GUgG)- gait columno dise works improve symptress and pathy of the GOAL in patients with TCC.

Methods: The 6-month dist intervention included 97 patients with UC, who were randomly divided into an intervention goog in = 49) and a control in - 40 group. Individual dist plans were created bit the intervention goog according to lgG bites; the control group cas haulthy div-an merant. Observitional index induced disease were; extrated intervention maniferations, neutrinon at these and QoA. Relationships between an merant. Observitional index induced mease area intervention; extinational maniferations, neutrinon at these load-spacific IoCi artifiedies and these indices were also antalyzed.

Results: At banding, then were no significant differences between the groups. Food-specific [gG antibodies were detected in 70,076 of parti-parts. Alter intervention, the Mayo score was applicately lower in the intervention group than is the control group (2.41 ± 0.09 vr 3.32 ± 1.1 perior new anomation, on many somession appending system to entrevening rough that is the control populated 2.2.209 (3), 22.2.13 Perior Distantion of policity with outwards maintainformation and the control population of the policy of the interpret of the policy of the intervening prop policy of the physics and both maintain the control prop (23.8.2.3) (23.8.2.4) (23.9

Conclusions: An IgG-prided occlasion diet antiferratiol UC symptoms and enproved QoL. Interactions between IgG and UC summit further study. Key Words: colinis, ulcorative, immanoglobulin G. food exclusion

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dok 16.1893/60/29130 Published online 18 May 2013

tion in grain quality of the (QoL)²¹ and may require libbing treatment. In addition to molection and suggery, detu man addition, and the intertuil an interboline.⁴ These reaction may UC: Therapeutic manuses should be baid on machanism UC: Therapeutic manuses should be baid on machanism that citologies, which are complex and uncertain in UC. Some Field indictance is in a deleyed or even maying that is delivered or manufacture in a delivery of even maying instance. researchers have proposed that UC is related to interactions

Received fat publications Networker 25, 2017; Editorial Distance February 23,

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INTRODUCTION between gat antigers and host immunity^{1, 2} When certain distribution of the state of the state

immune response to certain food antigens. It is mediated by immunoglobalin G (IgG), unlike food allergy, which is an IgEmediated immediate immune response. A retrospective study reported that patients with inflammatory bowel disease (IBD) had higher levels of IgG antibodies to specific food allergens than healthy people." That group speculated that the level of serum IgG may be related to disease status. Further studies have been performed to demonstrate that food-specific IgG guided exclusion dists improve symptoms in Croha's disease and that this approach may be useful in clinical practice.^{46,16} However although some prospective studies have focused on the effect of dietary components on the disease^{11,17} and other studies have withelimit(PB(455,ov)) 0.911 Cashi-& Cashi huadian do University of the statistical providence of the emains rarely reported in patients with UC. In 1962, Andresen reported that more than half of UC

patients benefited from a milk-free dist. Subsequent studies have intermittently reported the advantages of food exclusion

Jian L, Angi H, Gang L, et al. Food Exclusion Based on IgG Antibodies Alleviates Symptoms in Ulcerative Colitis: A Prospective Study, Inflamm Bowel Dis. 2018;24(9):1918-1925. doi:10.1093/ibd/izy110

Informing decisions Improving health

IgG Evaluation

- Literature review (2010) evaluating the validity of tests used to assess food reactions
- Food hypersensitivity, food allergy, food sensitivity, food intolerance testing and adverse food reactions
- IgG–based testing showed promise, with clinically meaningful results
- Proven useful as a guide for elimination diets
- Further investigation into the clinical application is required

Testing for Food Reactions: The Good, the Bad, and the Ugly	e 2 Percei
Gerard E. Mullin, MD ¹ ; Kathie M. Swift, MS, RD ² ; Liz Lipski, Laura K. Turnbull, BS, MSNe ⁴ ; and S. Devi Rampertab, MD ⁵ Finneid hidroine mus dictored.	PhD, CO
An increasing number of commercial tests for food allereise are alternative warditioners, unrus	uportabulin C

An increasing number of commercial tools for fload-linguise are maintained to consorts and handbare paratitioners with nonmatricial to consorts and handbare paratitioners with nonlased review of the tests and procedures that correctly are used for patients with empirical fload-allergy. A systematic review of the literature evoluting the solidity of tests and procedures and in fload braction was year formed using conventional starsh engines (e.g. Pabbod, Osal) as will are consumer which is Solider to the solidity of tests and prodening the solid procession was provided and the solid module of Solider testing, and adverse fload processivity was area doing with field allergy (essing, field strength or realistic solid procession) and the solid solid procession of fload allergy was best represented in Pabbod. [16] -sonklated toting continues to the the girld annulard for super-test fload dategings. Among modulus used by some consectional and

Techniques, Materials, Devices

alternative practitioners, nummenglobulin G (BgG)-based testing induced promotions, with chirachip meaningful results. It has here proven useful as a guide for climitation direct, with chiracal impact for a variety of directast. Mediator release testing and antigen ionizety: collubar antibady teering waver only repveated an ensumer sites. Further investigation trains due validity and the clinical application of these tests and provdense is required. Underlay the base for food resultions conductions in the content of an appropriate clinical history is and applied in the content of an appropriate clinical history is parameters in the adding the correct diagonsit. (New Clin Prox. 2010;21:192-198).

based Keywords: food sensitivity, food legaroensitivity, aller food and immunology, immunoglobalin E; immunoglobal d and G; skin tests

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available test results. In the context of the clinical history, both serum antibodies and allergy skin testing can be of considerable assistance in identifying (or excluding) the particular allergees that may be causing the partient's

From Johns Hupkins University School of Medicine, 'Carsons Banch-Lenos, MA, 'Hassthome University, Johns Hopkins University school of Surving, and 'Million S. Hershey Prun State University School of Medicine.

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sprotennes. Neureruss tests are available on the market and are being used by conventional and alternative practitioners to assess for food reactions. There are 2 main categories of tests available, allergy shift tests (skin prick testing) and measurements of allergo-specific antiholics from blood. We review the various tests along with the published evidence for find reactions for the classic ion.

Food Allergies

A food allergy is typically defined as an adverse immune response to the proteins in a food. This may occur as the result of a human dropponse limmanglobality. It full antibody), a cellular response (in Y cells), or both, tgl:melained food allergies affect between 1% and 2% of individuals in the U.S. and United Kingdown, specifically, how allergies are even in 1% of adults and 6%–8% of childrens. "The provolaces of food allergies in American children, according to the Centers for Dirasse Control end Provention." Certain foods are more common allergens among specific age groups. Accounting for the majority of immediate food allergies in syorary children with the control of the terms of the theory of the terms of the specific and provention.



Mullin GE, Swift KM, Lipski L, Turnbull LK, Rampertab SD. Testing for food reactions: the good, the bad, and the ugly. Nutr Clin Pract. 2010;25(2):192-198. doi:10.1177/0884533610362696

Informing decisions Improving health

- Much of the confusion surrounding the efficacy of food reaction testing, and non-IgE tests in particular, has arisen from indiscriminate use of the terms food allergy, and food intolerance and food sensitivity.
- Use of the term 'food allergy' to describe IgG food reactions has created the impression that functional and integrative physicians are equating IgE food allergies with IgG food reactions.
- This has led critics to dismiss IgG testing as lacking clinical utility because its results do not correlate with IgE tests.
- Unfortunately, this runs the very real risk of ignoring the relevance of IgG food reactions as a separate clinical condition.
- It discounts the progress that can be achieved through properly designed elimination diets for a variety of challenging health conditions.



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