



IgG Food Hypersensitivity and the ImuPro Dietary Concept

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Agenda

- **Immune vs. non-immune-mediated food hypersensitivity**
- **The evidence base for IgG food testing**
- **The ImuPro test**
- **The exclusion criteria**
- **Individualised recipes**
- **The ImuPro strategy suggested:**
 - **Exclusion**
 - **Provocation**
 - **Stabilisation**

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Adverse reactions to foods are primarily classified into non-immune and immune mediated reactions

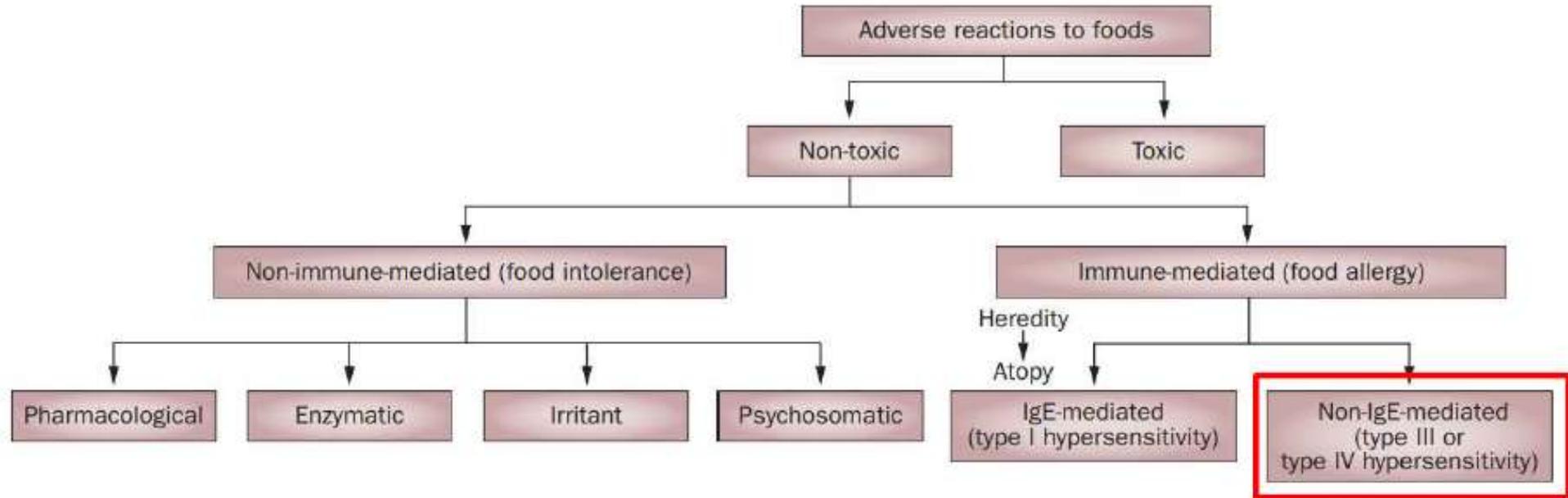


Figure 1 | Classification of adverse reactions to foods according to pathogenic mechanisms.⁹ Two main entities of adverse reactions to food exist: toxic and non-toxic reactions. The latter comprises pathogenic mechanisms that are both immune-mediated and non-immune-mediated. Non-immune-mediated mechanisms include pharmacological, enzymatic and unclear causes, such as certain irritants and psychosomatic responses. The IgE-mediated reactions constitute type I hypersensitivity while the non-IgE-mediated reactions are tentatively deemed to be type III hypersensitivity (IgG or IgM immune complex reactions) or type IV hypersensitivity (delayed-type or cell-mediated reactions). Atopy is the hereditary trait of producing excessive levels of IgE antibodies, therefore predisposing to type I hypersensitivity (Box 1).

Non-immune mediated food hypersensitivity



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Food Allergy



Foods Involved

Vaccines and Food Allergy

Management

Allergy Prevention

Non-IgE-mediated food allergy

Mechanisms

Investigations

▶ Non-immune mediated food hypersensitivity

Non-immune mediated food hypersensitivity

Enzyme reactions

The most common presentation of reactions to foods due to enzyme deficiencies, is lactose intolerance. This involves abdominal pain, bloating, diarrhoea, flatulence and occasionally nausea and vomiting after ingesting milk, due to a deficiency of the enzyme lactase. Lactose intolerance is most prevalent in people of Indian, South American or African heritage. A history of gastro-intestinal symptoms linked to milk is a useful guide and a 4-week exclusion of milk and milk products followed by symptom improvement may be diagnostic. A diagnosis can also be reached by performing a hydrogen breath test, which has good sensitivity and specificity. A test is considered to be positive if the breath hydrogen level is ≥ 20 ppm above baseline and/or methane is ≥ 15 ppm. Intolerance to fructose, the sugar in fruit, honey and some syrups, should be considered if symptoms persist despite exclusion of lactose, or if a lactose breath test is negative.

Enzyme reactions, pharmacological reactions, irritants (e.g. food additive reactions), lack of psychological tolerance

Source: <https://www.bsaci.org/professional-resources/allergy-management/food-allergy/non-immune-mediated-food-hypersensitivity/>

Immune-mediated food hypersensitivity: one type is IgE-mediated food allergy

IgE mediated food allergies

- * Risk of anaphylaxis.
- * Hives.
- * Swelling of mouth, lips or throat.
- * Difficulty breathing.
- * Could be fatal.
- * Treat with epipen.



Using NHS Data to monitor trends in the occurrence of severe, food induced allergic reactions

Around 3% of the UK population have IgE-mediated food allergy and are at risk of potentially life-threatening allergic reactions. An inability to identify those most at risk of truly severe anaphylaxis and the circumstances leading to such reactions represents an important knowledge gap. This project seeks to better understand these issues.



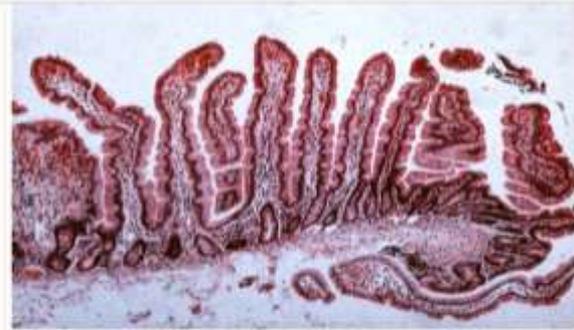
Source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5123910/>; <https://www.food.gov.uk/research/food-hypersensitivity#:~:text=Around%203%25%20of%20the%20UK,potentially%20life%2Dthreatening%20allergic%20reactions;> <https://www.allergyuk.org/types-of-allergies/food-allergy/>; <https://naturopathicpediatrics.com/2017/02/10/understanding-food-allergy-food-sensitivity-iga-igg-ige/>

Immune-mediated disorder: coeliac disease

“The disease is produced by an immune-mediated enteropathy triggered by ingested prolamins present in wheat, barley, and rye (generically called gluten) occurring in predisposed individuals carrying the characteristic HLA haplotype DQ2 and/or DQ8.”

Table 1: Cereal Sources of Gluten

- Wheat
- Wheatberries
- Rye
- Barley
- Spelt
- KAMUT®
- Triticale
- Durum Wheat or Semolina
- Club Wheat
- Emmer
- Einkorn
- Farro



Photograph 1: Photomicrograph of the normal small intestinal lining; note the villi that protrude into the intestinal lumen and absorb nutrients.



Photograph 2: Photomicrograph of the small intestinal lining from a patient with untreated celiac disease: note the absence of villi - the so-called 'flat lesion'

Immunoglobulin G – one of the most abundant proteins in human serum: 10-20% of plasma protein



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Volume 5 - 2014 | <https://doi.org/10.3389/fimmu.2014.00520>[View all 13 Articles >](#)

IgG subclasses and allotypes: from structure to effector functions

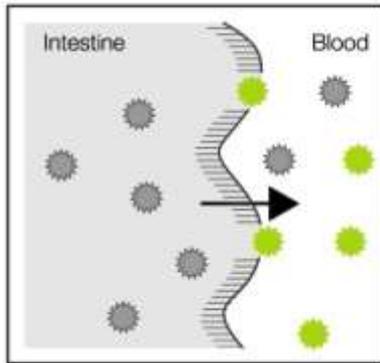
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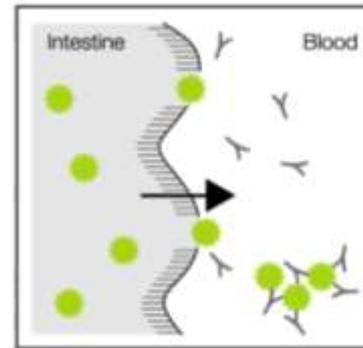
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Of the five immunoglobulin isotypes, immunoglobulin G (IgG) is most abundant in human serum. The four subclasses, IgG1, IgG2, IgG3, and IgG4, which are highly conserved, differ in their constant region, particularly in their hinges and upper CH2 domains. These regions are involved in binding to both IgG-Fc receptors (FcγR) and C1q. As a result, the different subclasses have different effector functions, both in terms of triggering FcγR-expressing cells, resulting in phagocytosis or antibody-dependent cell-mediated cytotoxicity, and activating complement. The Fc-regions also contain a binding epitope for the neonatal Fc receptor (FcRn), responsible for the extended half-life, placental transport, and bidirectional transport of IgG to mucosal surfaces. However, FcRn is also expressed in myeloid cells, where it participates in both phagocytosis and antigen presentation together with classical FcγR and complement. How these properties, IgG-polymorphisms and post-translational modification of the antibodies in the form of glycosylation, affect IgG-function will be the focus of the current review.

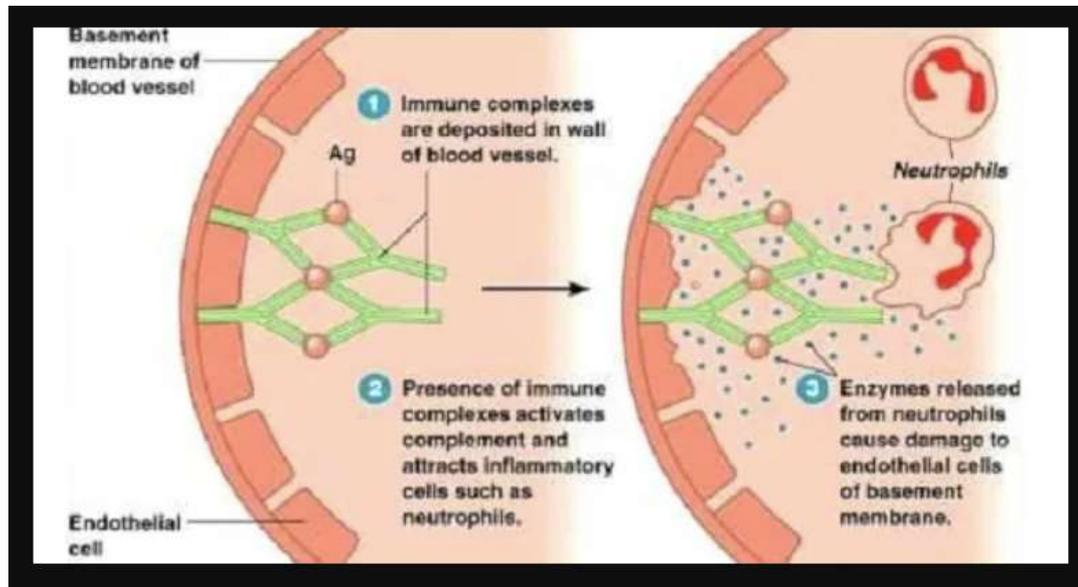
Immune complexes form that trigger inflammatory reactions and eventually tissue damage



Intestinal wall is damaged:
food components can slip
between intestinal cells.



Immune reaction:
formation of immune
complexes.



“In type III hypersensitivity reactions, an abnormal immune response is mediated by the formation of antigen-antibody aggregates called "immune complexes." [1] They can precipitate in various tissues such as skin, joints, vessels, or glomeruli and trigger the classical complement pathway. Complement activation leads to the recruitment of inflammatory cells (monocytes and neutrophils) that release lysosomal enzymes and free radicals at the site of immune complexes, causing tissue damage.”

Further ramifications of this tissue damage

Development, structure, and function of the intestinal epithelial barrier

Go to: ▶

The main function of the intestinal barrier is to regulate the absorption of nutrients, electrolytes and water from the lumen into the circulation and to prevent the entry of pathogenic microorganisms and toxic luminal substances (Farhadi et al., [2003](#)). Furthermore, regulation of the exchange of molecules between the environment and the host through the intestinal barrier influences the equilibrium between tolerance and immunity to self and non-self-antigens (Fasano and Shea-Donohue, [2005](#); Fasano, [2011](#)). From a structural perspective these functions are preserved by a number of features including a mucus layer and a monolayer of epithelial cells interconnected by tight junctions (Madara, [1998](#)). The mucus layer containing secretory immunoglobulin (Ig) A and antimicrobial peptides covers the epithelial cell lining which functions to facilitate GI transport, and as a protective layer against bacterial invasion. The colonic mucus layer is composed of two layers, an outer and inner layer composed of gel forming highly glycosylated proteins termed mucins. These are produced and maintained by goblet cells which renew the inner mucus layer approximately every hour (Johansson et al., [2011](#)). These dynamic processes are subject to extensive and continuous interplay with the gut microbiota, disruption of which may have implications for the sustenance of key barrier functions (Yu et al., [2012](#); Bischoff et al., [2014](#)).

Tight junctions on the other hand are complex protein structures that consist of transmembrane proteins such as claudin, occludin, and tricullulin (Dörfel and Huber, [2012](#)). These transmembrane proteins connect with the opposing plasma membrane, thereby forming a mechanical link between epithelial cells and establishing a barrier to paracellular diffusion of fluid and solutes (Tran et al.

The intestinal barrier is supposed to prevent the entry of pathogenic microorganisms into the circulation: if compromised, it potentially acts as a door to rolling infection

Mitochondrial dysfunction deeply involved due to the ensuing inflammation – a vicious cycle begins

Review > FEBS J. 2020 Aug;287(16):3350-3369. doi: 10.1111/febs.15327. Epub 2020 Apr 27.

Glycolysis – a key player in the inflammatory response

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Abstract

The inflammatory response involves the activation of several cell types to fight insults caused by a plethora of agents, and to maintain the tissue homeostasis. On the one hand, cells involved in the pro-inflammatory response, such as inflammatory M1 macrophages, Th1 and Th17 lymphocytes or activated microglia, must rapidly provide energy to fuel inflammation, which is essentially accomplished by glycolysis and high lactate production. On the other hand, regulatory T cells or M2 macrophages, which are involved in immune regulation and resolution of inflammation, preferentially use fatty acid oxidation through the TCA cycle as a main source for energy production. Here, we discuss the impact of glycolytic metabolism at the different steps of the inflammatory response. Finally, we review a wide variety of molecular mechanisms which could explain the relationship between glycolytic metabolites and the pro-inflammatory phenotype, including signalling events, epigenetic remodelling, post-transcriptional regulation and post-translational modifications. Inflammatory processes are a common feature of many age-associated diseases, such as cardiovascular and neurodegenerative disorders. The finding that immunometabolism could be a master regulator of inflammation broadens the avenue for treating inflammation-related pathologies through the manipulation of the vascular and immune cell metabolism.

Keywords: ageing; immune cells; immunometabolism; inflammation; metabolites.

“Cells involved in the pro-inflammatory response, such as inflammatory M1 macrophages, Th1 and Th17 lymphocytes or activated microglia, must rapidly provide energy to fuel inflammation, which is essentially accomplished by glycolysis and high lactate production.”

Source: Soto-Herederó G, Gómez de Las Heras MM, Gabandé-Rodríguez E, Oller J, Mittelbrunn M. Glycolysis - a key player in the inflammatory response. FEBS J. 2020 Aug;287(16):3350-3369.

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IgG food hypersensitivity can cause a wide range of disorders

- Gastrointestinal symptoms:
 - Crohn's disease
 - Diarrhoea
 - Irritable Bowel Syndrome (IBS)
 - Inflammatory Bowel Disease (IBD)
- Skin-related issues:
 - Dermatitis
 - Eczema
 - Psoriasis
 - Rashes
- Chronic pain, headaches, migraine
- Excess weight/chronic weight issues
- Autoimmune conditions

Large evidence base for IgG hypersensitivity causing inflammation

Immunology and inflammation

Selection, not exhaustive

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... as well as in IBD ...

Selection, not exhaustive

Inflammatory bowel disease

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... and IBS – all of the D, C and M varieties

Selection, not exhaustive

Inflammatory bowel syndrome

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Value in migraine and IBD

Randomized Controlled Trial > Headache. 2013 Mar;53(3):514-25.

doi: 10.1111/j.1526-4610.2012.02296.x. Epub 2012 Dec 6.

IgG-based elimination diet in migraine plus irritable bowel syndrome

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Affiliations + expand

PMID: 23216231 DOI: 10.1111/j.1526-4610.2012.02296.x

Abstract

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 allergens 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.

Conclusions: 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

Randomised controlled trial

“Conclusions: 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.”

Improved migraine symptoms and quality of life

Open Journal of Internal Medicine, 2013, 3, 8-14
<http://dx.doi.org/10.4236/ojim.2013.31003> Published Online March 2013 (<http://www.scirp.org/journal/ojim/>)

OJIM

Pilot study

A pilot study eliminating immunologically-reactive foods from the diet and its effect on symptomatology and quality of life in persons with chronic migraines and headaches*

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ABSTRACT

Purpose: Chronic migraines and headaches are significant public health problems, and their symptomatology has been positively linked to diet. We explored if individuals suffering from chronic migraines/headaches who required medication treatment had improvement in symptomatology and subjective ratings of QoL when following an immune-reactive food exclusion diet based on the results of the ImmunoBlood-print test, an IgG-mediated food sensitivity assay. **Methods:** Thirty-seven subjects, aged 18 and over, took part in the study. Subjects had to eliminate all reactive foods from their diet for 90 days. Migraine intensity and frequency were measured using the MTAQ, and QoL was assessed with the SF-36 survey at baseline and 30-, 60-, and 90-day follow-up. **Results:** Subjects who eliminated IgG-mediated reactive foods from

1. INTRODUCTION

Headaches and migraines affect 46% of the global adult population, and they constitute a significant public health issue given their negative effect on quality of life (QoL) and resulting level of disability [1,2]. Migraines/headaches are multifactorial and involve several different predispositions, the influences of which vary for each individual person. However, many studies positively link diet to symptomatology. Studies have indicated that the percent of patients reporting food as a trigger for migraines range from 12% - 60% with many of them reporting more than one food [3-5]. For example, one study evaluated triggers of migraine without aura in 100 subjects and found that in 20 patients migraines were occasionally triggered by foods like chocolate, cheese, wine, tomatoes, nuts, carbonated beverages, and leavened products [6]. Therefore, an individualized diet to relieve mi-



“Results: [37] Subjects who eliminated IgG-mediated reactive foods from their diet had reductions in migraine symptomatology and had improvements in nearly all indicators of QoL, according to the SF-36, from baseline to 90-day follow-up. Conclusions: Subjects were able to improve their migraine symptoms and QoL in response to eliminating IgG reactive foods from the diet. This test may represent a strategy to help mediate chronic migraine symptomatology without the use of medication.”

Effective strategy in reducing the frequency of migraine attacks



Cephalalgia, 2010 Jul; 30(7): 829–837.
doi: [10.1177/0333102410361404](https://doi.org/10.1177/0333102410361404)

PMCID: PMC2899772
PMID: [20847174](https://pubmed.ncbi.nlm.nih.gov/20847174/)

Double-blind randomised cross-over trial

Diet restriction in migraine, based on IgG against foods: A clinical double-blind, randomised, cross-over trial

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Abstract

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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.

Keywords: migraine, food, diet, IgG, trigger

“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.”

Significant improvements in abdominal pain and diarrhoea



The Journal of International Medical Research
2012; 40: 204 – 210 [first published online ahead of print as 40(1) 1]

The Value of Eliminating Foods According to Food-specific Immunoglobulin G Antibodies in Irritable Bowel Syndrome with Diarrhoea

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OBJECTIVE: This study investigated the role of food intolerance in irritable bowel syndrome with diarrhoea (D-IBS). **METHODS:** Specific immunoglobulin G (IgG) antibodies against 14 common food antigens in the serum were measured in 77 patients with D-IBS and 26 healthy controls. Food-specific IgG antibodies were identified in 39 (50.65%) patients with D-IBS compared with four (15.38%) controls. For 12 weeks following the serological testing, 35 patients with D-IBS and food intolerance consumed diets that excluded the identified food. Changes in the main symptoms of D-

IBS were evaluated before treatment and regularly during treatment in these patients. **RESULTS:** After 4 weeks' dietary therapy, most symptoms of D-IBS had improved. By 12 weeks, all symptom scores had decreased significantly compared with the baseline scores. **CONCLUSIONS:** The 12-week specific-food exclusion diets resulted in significant improvements in abdominal pain (bloating level and frequency), diarrhoea frequency, abdominal distension, stool shape, general feelings of distress and total symptom score compared with baseline in patients with D-IBS.

KEY WORDS: IRRITABLE BOWEL SYNDROME WITH DIARRHOEA; FOOD INTOLERANCE; IMMUNOGLOBULIN G ANTIBODIES; DIET THERAPY; ABDOMINAL SYMPTOMS

Introduction

Irritable bowel syndrome (IBS) is a chronic functional bowel disorder with an increasing global incidence rate.¹⁻⁸ IBS affects people's quality of life to varying degrees and uses a

variety of foods that increase their immunoglobulin G (IgG) antibody levels, their gastrointestinal tract symptoms reduce significantly.¹⁶⁻¹⁸ Some physicians remain

77 p/ts with D-IBS and 26 healthy controls
Conclusions: The 12-week specific-food exclusion diets resulted in significant improvements in abdominal pain (bloating level and frequency), diarrhoea frequency, abdominal distension, stool shape, general feelings of distress and total symptom score compared with baseline in patients with D-IBS

Can improve body composition and quality of life



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Research Article Open Access

Eliminating Immunologically-Reactive Foods from the Diet and its Effect on Body Composition and Quality of Life in Overweight Persons

John E. Lewis^{1*}, Judi M. Woolger², Angelica Melillo¹, Yaima Alonso², Soyona Rafatjah², Sarah A. Jones¹, Janet Konefal¹, Amine Sarabia¹, Susanna Leonard¹, Evan Long¹, Nicole Quicuti¹, Kathy Gonzalez¹ and Jared Tannenbaum¹

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Abstract

Background: Given the relationship between chronic disease and poor nutritional habits, using strategies to address the crisis of poor health in the U.S. is necessary. We explored if overweight people wanting to lose weight could benefit from having the Immuno Bloodprint, a proprietary IgG-mediated food sensitivity test to determine which foods to eliminate from the diet. IgG-mediated antibodies are thought to be causal in some food hypersensitivity and thus related to overweight status.

Objective: This study assessed the effect of an IgG-mediated food sensitivity test in combination with a food elimination diet on body composition and secondary outcomes in people who wanted to lose weight and/or were overweight.

Methods: A total of 120 subjects aged 18 and over took part in the study. Subjects had to eliminate all reactive foods from their diet for 90 days. Body composition, blood pressure and pulse, and quality of life were assessed at baseline and 30-, 60-, and 90-day follow-up.

Results: Subjects who eliminated IgG-mediated reactive foods from their diet had reductions in weight, body mass index, waist and hip circumferences, resting diastolic blood pressure and had improvements in all indicators of quality of life according to the SF-36 from baseline to 90-day follow-up.

Conclusions and Context: Subjects were able to improve their body composition and quality of life in response to eliminating IgG reactive foods from the diet. This test may represent a strategy to counteract the severe U.S. obesity epidemic.

“[120] Subjects were able to improve their body composition and quality of life in response to eliminating IgG reactive foods from the diet. This test may represent a strategy to counteract the severe U.S. obesity epidemic.”

Significant improvements in all thyroid markers



A six-month observational/
interventional study

Article

The Influence of Reducing Diets on Changes in Thyroid Parameters in Women Suffering from Obesity and Hashimoto's Disease

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Abstract: Hashimoto's disease is listed among the most common endocrine causes of obesity. As treatment of obesity in women with Hashimoto's disease is frequently unsuccessful, the aim of this study was to evaluate the effectiveness of two different reducing diets and their influence on changes in thyroid parameters in female patients. A six-month observational/interventional study was performed on 100 women aged 18–65 years, previously diagnosed with Hashimoto's disease and obesity and receiving L-thyroxine. The women were randomly assigned to the test group (group A, $n = 50$) following elimination/reducing diets, and the control group (group B, $n = 50$) following reducing diets with the same caloric content (without elimination). Anthropometric and thyroid parameters were evaluated at the beginning, after 3 months and after 6 months of treatment. In both groups a significant decrease in BMI and body fat percentage was achieved, but in test group A the decrease in BMI and body fat percentage was significantly greater than in control group B ($p < 0.002$ and $p = 0.026$, respectively). Serum TSH (thyroid stimulating hormone) levels decreased significantly more in group A than in group B ($p < 0.001$). Group A exhibited significantly greater increases in fT4 and fT3 levels than the control group ($p < 0.001$) as well as significantly greater decreases in the levels anti-TPO (thyroid peroxidase) ($p < 0.001$) and anti-TG (thyreoglobulin) antibodies ($p = 0.048$). The application of reducing diets with product elimination was found to be a more beneficial tool for changing anthropometric and thyroid parameters in women suffering from obesity and Hashimoto's disease than classic reducing diets with the same energy values and macronutrient content.



Citation: Ostrowska, L.; Gier, D.; Zyśk, B. The Influence of Reducing Diets on Changes in Thyroid Parameters in Women Suffering from Obesity and Hashimoto's Disease. *Nutrients* **2021**, *13*, 862. <https://doi.org/10.3390/nu13030862>

“In test group A the decrease in BMI and body fat percentage was significantly greater than in control group B ($p < 0.002$ and $p = 0.026$, respectively). **Serum TSH (thyroid stimulating hormone) levels decreased significantly more in group A than in group B ($p < 0.001$).** Group A exhibited **significantly greater increases in fT4 and fT3 levels than the control group ($p < 0.001$)** as well as **significantly greater decreases in the levels anti-TPO (thyroid peroxidase) ($p < 0.001$) and anti-TG (thyreoglobulin) antibodies ($p = 0.048$).**”

Source: Ostrowska L, Gier D, Zyśk B. The Influence of Reducing Diets on Changes in Thyroid Parameters in Women Suffering from Obesity and Hashimoto's Disease. *Nutrients*. 2021 Mar 5;13(3):862.

Agenda

- Immune vs. non-immune-mediated food hypersensitivity
- The evidence base for IgG food testing
- **The ImuPro test**
- The exclusion criteria
- Individualised recipes
- The ImuPro strategy suggested:
 - Exclusion
 - Provocation
 - Stabilisation

Four types of IgG: important to measure all 4, and ImuPro does

	IgG1		IgG2		IgG3		IgG4	
General								
Molecular mass (kD)	146		146		170		146	
Amino acids in hinge region	15		12		62 ^a		12	
Inter-heavy chain disulfide bonds	2		4 ^b		11 ^a		2	
Mean adult serum level (g/l)	6.98		3.8		0.51		0.56	
Relative abundance (%)	60		32		4		4	
Half-life (days)	21		21		7/~21 ^a		21	
Placental transfer	++++		++		++/++++ ^a		+++	
Antibody response to:								
Proteins	++		+/-		++		++ ^a	
Polysaccharides	+		+++		+/-		+/-	
Allergens	+		(-)		(-)		++	
Complement activation								
C1q binding	++		+		+++		-	
Fc receptors								
FcγRI	+++ ^c	65 ^d	-	-	++++	61	++	
FcγRIIa _{H131}	+++	5.2	++	0.45	++++	0.89	++	
FcγRIIa _{R131}	+++	3.5	+	0.10	++++	0.91	++	
FcγRIIb/c	+	0.12	-	0.02	++	0.17	+	
FcγRIIIa _{F158}	++	1.2	-	0.03	++++	7.7	-	
FcγRIIIa _{V158}	+++	2.0	+	0.07	++++	9.8	++	
FcγRIIIb	+++	0.2	-	-	++++	1.1	-	
FcRn (at pH < 6.5)	+++		+++		++/++++ ^a		+++	

^aDepends on allotype.

^bFor A/A isomer.

IgG 1 60%

IgG 2 32%

IgG 3 4%

IgG 4 4%

Test can be conducted either as a blood draw or a fingerprick test



Capillary blood material requirements

for ImuPro tests (with Whatman card):

270 antigens: 5 completely filled circles of blood

180 antigens: 5 completely filled circles of blood

90 antigens: 4 completely filled circles of blood

44 antigens: 2 completely filled circles of blood

RIDASCREEN Foodscreen Blood Collection Kit



The Blood Collection Kit is meant for the sampling and transport of human blood samples
The antibodies will be eluted from the Blood Collection Card
The eluted antibodies can be used as alternative for diluted serum samples



Different types of test available, including vegetarian

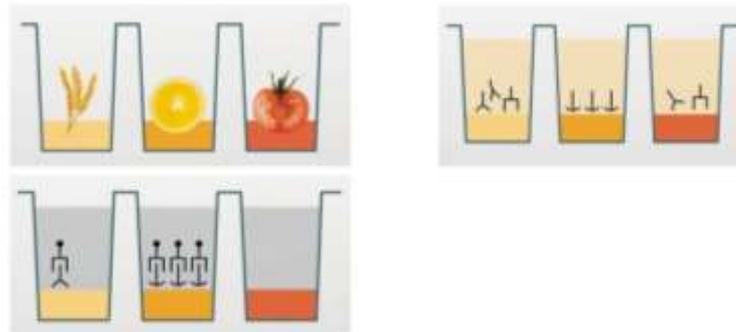
Food allergy type III (IgG)		Material
<input type="checkbox"/>	ImuPro Complete 270 Food antigens - recipe book is included	S/C
<input type="checkbox"/>	ImuPro Basic Plus 180 Food antigens - recipe book is included	S/C
<input type="checkbox"/>	ImuPro Basic 90 Food antigens - without recipe book	S/C
<input type="checkbox"/>	ImuPro Screen Plus 44 Food antigens - without recipe book	S/C
<input type="checkbox"/>	ImuPro Vegi Plus 221 Food antigens, vegetarian - recipe book is included	S/C
<input type="checkbox"/>	ImuPro Vegi 90 Food antigens, vegetarian - without recipe book	S/C
<input type="checkbox"/>	Upgrade ImuPro Basic → ImuPro Complete (90 → 270 Food antigens) within 4 weeks - recipe book is included	S/C



The testing process in the lab

The procedure involves looking for delayed immune reactions that start 3 – 72 hours after an antigen has been consumed. The antibodies are isolated from the patient's blood and brought into contact with food proteins under the guidance and supervision of a specialist laboratory doctor.

The lab process ImuPro involves specific proteins extracted from up to 270 foods using a special processing method. These 270 different protein solutions are then applied to the still empty plates in separate wells.



The patient's blood is then placed in each well of the test panel. The wells contain the specific food proteins. The IgG antibodies in the blood sample bind to the appropriate food proteins (or allergens), e.g. antibodies against wheat only bind in the well containing wheat proteins. An antibody against IgG is then applied to each plate. The new antibody binds to the ends of the existing IgG antibodies and if there are antibodies present, an enzyme at the end of the antibody produces a colour reaction.

The items are arranged by category, which enables a good overview

List 1 - Individual laboratory result

ImuPro Complete

	µg/ml IgG	Rating	Additional exclusions		µg/ml IgG	Rating	Additional exclusions
Cereals containing gluten				Meat			
Barley*	7,0			Beef	6,2		
Gluten	33,4			Chicken	2,6		
Kamut	24,6			Deer	< 2,5		
Rye*	14,4			Duck	2,8		
Spelt	30,6			Goat	5,2		
Wheat	30,1			Goose	< 2,5		
Cereals w/o gluten and alternatives				Hare			
Amaranth	< 2,5			Lamb	14,4		
Arrowroot	< 2,5			Ostrich	< 2,5		
Buckwheat	4,1			Pork	7,3		
Carob	7,1			Quail	< 2,5		
Cassava	3,2			Rabbit	< 2,5		
Fonio	11,5			Turkey	< 2,5		
Jerusalem artichoke	2,8			Veal	4,9		
Lupine	4,0		HI	Venison	< 2,5		
Maize, sweet corn	18,2			Wild boar	4,9		
Millet	7,5			Milk products			
Oats	10,2			Camel's milk	35,1		
Quinoa	4,5			Goat: milk / cheese	34,8		
Rice	5,2			Halloumi	11,6		
Sweet chestnut	3,4			Kefir	27,0		
Sweet potato	2,7			Mare's milk	10,2		
Tapioca	< 2,5			Milk (cow)	36,5		
Teff	18,3			Milk (cow, cooked) ¹	29,0		
Eggs				Rennet cheese (cow)			
Chicken egg white	187,5			Ricotta	33,7		
Chicken egg yolk	21,8			Sheep: milk / cheese	31,6		
Goose eggs	30,6			Sour-milk prod. (cow)	32,6		HI
Quail eags	34,2						

¹ The tested cow's milk was boiled for 30 min, cooled and the resulting skin

- Cereals containing gluten
- Cereals without gluten and alternatives
- Eggs
- Meat
- Milk products
- Fruits
- Seeds and nuts
- Salads
- Vegetables
- Spices and herbs
- Fish and seafood
- Teas, coffee and tannin
- Yeast
- Mushrooms
- Specials
- Algae
- Sweeteners
- Food additives

The more antibodies in a well, the stronger the colour

Watermelon	11,7		
Yellow plum	< 2,5		
Seeds and nuts			
Almond	68,0		NU
Brazil nut	4,1		NU
Cashew kernels	10,8		NU
Cocoa bean	11,0		HI
Coconut	4,3		
Hazelnut	5,7		HI, NU
Linseed	5,6		
Macadamia nut	10,9		NU
Peanut	181,0		HI, NU
Pine nut	< 2,5		
Pistachio	19,9		NU
Poppy seeds	3,1		
Pumpkin seeds	9,1		
Sesame	7,0		HI
Sunflower seed	16,6		
Walnut	5,7		HI, NU

	µg/ml IgG	Rating
Food 1	5	
Food 2	7	
Food 3	77	

Based on the results of the antibody titre, the foods are categorised into three groups:

Not elevated (green)

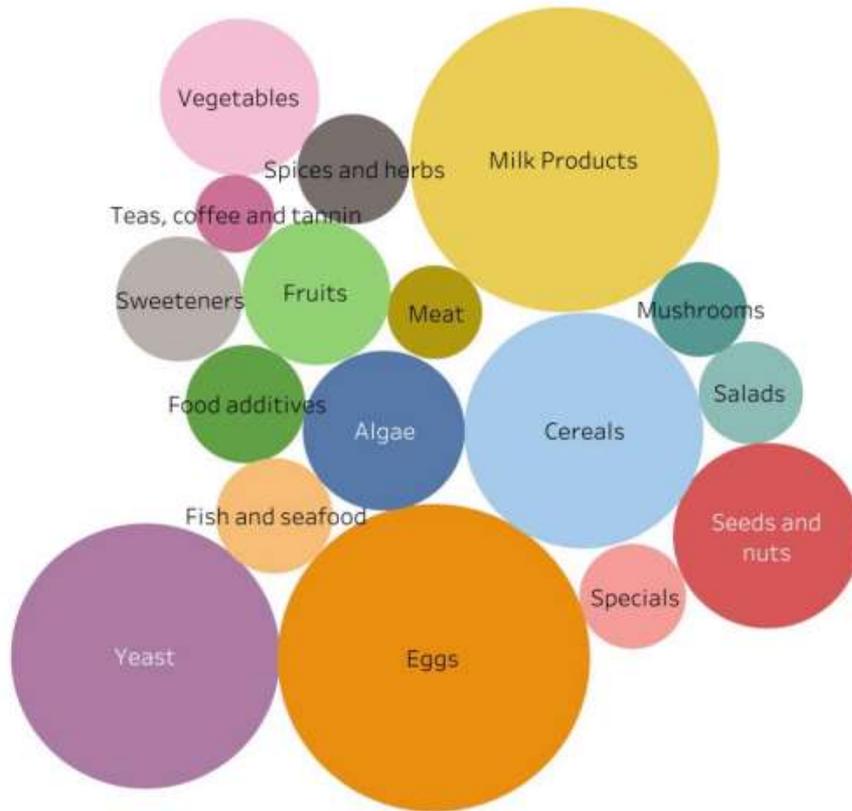
elevated (orange)

highly elevated (red)

The exact level is also given in µg/ml IgG, and in some cases the upper range of “normal” is also relevant

Study amongst 1644 participants found IgG reactivity was predominant in eight foods

Alkhateeb; ARRB, 35(3): 115-127, 2020; Article no.ARRB.57330



“IgG reactivity was predominant in eight foods (3%) in at least three-quarters of the studied population. These included Oats (82.5%), Barley (79.1%), Rye (76.1%) Cow’s Milk (75%), Wheat (74.9%), Kamut (74.6%), Spelt (74.6%) and Gluten (73.9%). The IgG immune response of males and females to each food type was found to be almost the same.”

Fig. 1. Food groups causing IgG immune reaction. The size of the circle indicates the percentage of the population affected by this food group

Studies have evidenced zero physiological increase in IgG titres after provocation with foods high up in those categories*

In a study to estimate the probability of developing IgG antibodies to certain foods, the Institute for Microecology in Herborn, Germany performed the following study: 25 subjects who had no IgG to soy, hen's egg and cow's milk were divided into 3 subgroups. Group 1 added 750 ml of cow's milk to their daily diet, Group 2 introduced 2 eggs per day, and Group 3 drank 750ml of soy milk daily for 3 weeks. After 3 weeks their respective titer of IgG was determined and again after 4 weeks. Result: none of the 25 subjects developed any IgG to the foods consumed.

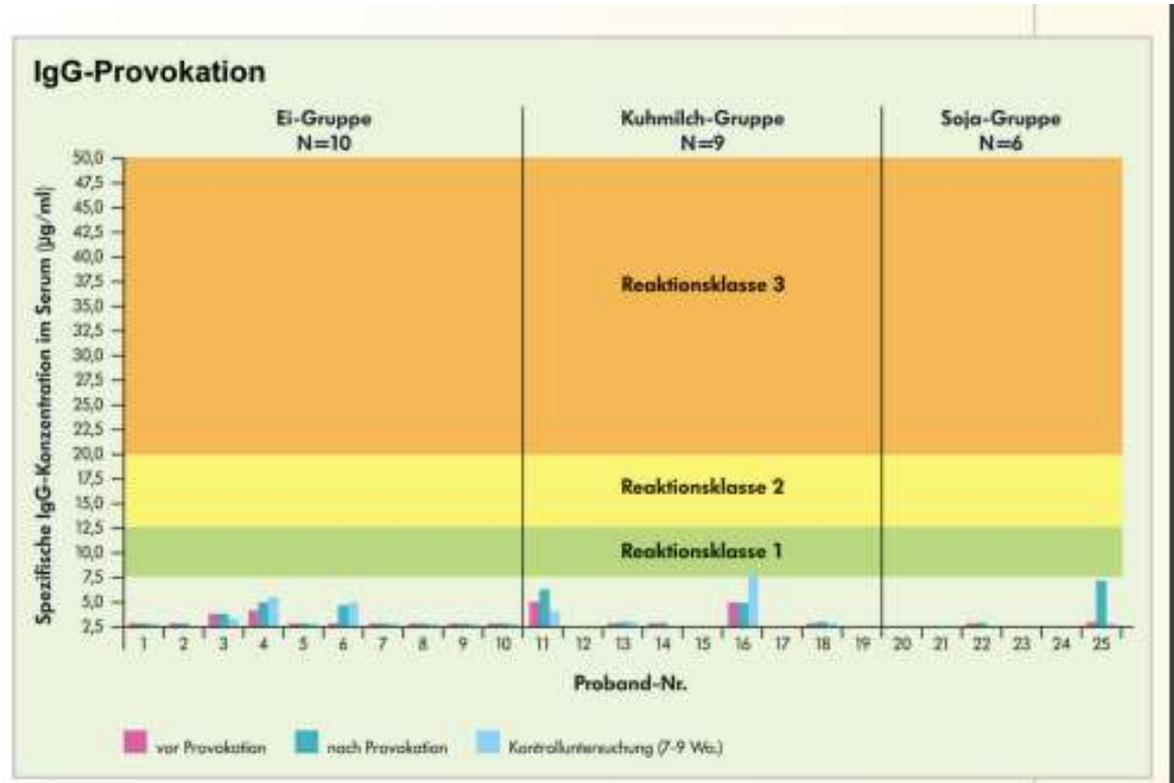
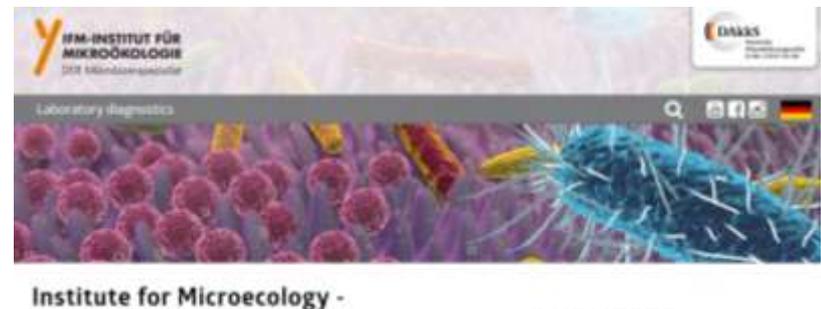


Fig. 2 IgG values before, immediately after and 4-6 weeks after provocation

* In individuals who are not suffering from any perceived hypersensitivity to those foods

Source: IgG-Diagnostik: kein physiologischer Titeranstieg nach Lebensmittelverzehr.
Kerstin Rusch, Ernährungsmedizin, Medical spezial 1/2010



Agenda

- Immune vs. non-immune-mediated food hypersensitivity
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16 additional exclusion categories – plus “other”

Indicate below **3 categories that you would like to be excluded** from the list of recommended foods/recipe book/rotation diet even if you do not have an IgG reaction to these foods. (This would be because you know you do not wish these foods to be included in your/your patient’s diet, e.g., because of wanting to avoid gluten, or dairy. Please mark the box(es) as appropriate:

Note: Please state a maximum of 3 exclusion criteria. (Subsequent statements and reissue of recipe books and findings are subject to a charge of £12)

Please note that the number of available recipes is reduced with each exclusion criterion.

- | | | | |
|---|---|---|--|
| <input type="checkbox"/> Foods with high histamine content (HI) | <input type="checkbox"/> Cereals containing gluten (GL) | <input type="checkbox"/> Seafood (Shellfish & Crustaceans) (SK) | <input type="checkbox"/> Fish (FI) |
| <input type="checkbox"/> Foods containing lactose (LA) | <input type="checkbox"/> Foods containing fructose (FR) | <input type="checkbox"/> Nuts (NU) | <input type="checkbox"/> Cabbage varieties and other cruciferus (KO) |
| <input type="checkbox"/> All non-vegetarian food (VE) | <input type="checkbox"/> All non-vegan food (VN) | <input type="checkbox"/> Mushrooms (PI) | <input type="checkbox"/> Citrus fruits (ZI) |
| <input type="checkbox"/> Foods containing lectin (LE) | <input type="checkbox"/> Legumes (HU) | <input type="checkbox"/> Stone fruit (ST) | <input type="checkbox"/> Foods containing sorbitol (SO) |
| <input type="checkbox"/> Other: _____ | | | |

Fish and seafood			
Anchovy	4,7	4,5 9	HI
Angler, monkfish	5,7	9,5 19	
Blue mussels	7,4	10,9 21,8	HI
Carp	9,1	7,5 15	
Cod, codling	< 2,5	7,8 15,6	
Crayfish	< 2,5	6,1 12,2	HI
Eel	4,1	6,4 12,8	
Gilthead bream	6,4	4,6 9,2	
Haddock	8,4	7,2 14,4	
Hake	2,5	7,5 15	
Halibut	2,5	4,2 8,4	
Herring	3,0	7,5 15	
Iridescent shark	6,8	19,8 39,2	
Lobster	8,6	15,2 21,5	HI
Mackerel	5,4	8,1 16,2	HI
Ocean perch	5,7	8,8 17,5	
Octopus	4,2	11,9 23,8	HI
Oysters	11,6	18 36	HI

Seeds and nuts			
Almond	68,0	27 51,9	NU
Brazil nut	4,1	16,5 32,3	NU
Cashew kernels	10,8	23,4 46,1	NU
Cocoa bean	11,0	10,4 20,8	

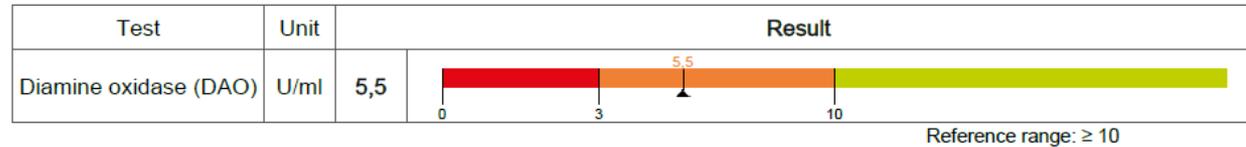
Histamine add-on very useful, too

Martina Musterfrau
date of birth: 12.07.1994 / age: 28 / sex: f / sample id: 333333



Histamine intolerance test (HIT)

14.06.2023



Interpretation:

DAO concentration is reduced to borderline levels. Histamine intolerance is presumed.
Please note the therapeutic recommendation stated below.

GENERAL RECOMMENDATIONS

Elimination diet: Avoiding the foodstuffs according to the ImuPro food list.

In addition, you should avoid the following processed food which is relevant to histamine intolerance: alcoholic beverages, in particular red wine, champagne, wheat beer; products containing cocoa (chocolate, sweets, biscuits, desserts); salami and other raw sausages and cold cuts (cervelat, Kantwurst [Austrian type of salami], Osso collo, Westphalian ham); products containing tomatoes (ketchup); Sauerkraut; Wheat sprouts; vinegar, in particular red wine vinegar, table vinegar; yeast extract; fish if stored for a while or if cold chain interrupted, if smoked, cured (fresh fish contains almost no histamine).

The tolerance thresholds of patients vary and must thus be determined individually by testing. The same applies for the taking of diamine oxidase-inhibiting drugs or alcohol.

Substitution: The possibilities of substituting diaminooxidase with enzyme preparations of animal (e.g. DAOSiN, DAOfood) or plant origin (e.g. NaturDAO, DAOfood veg)[®] should be discussed with your physician or therapist.

Inadequate histamine degradation is frequently missed

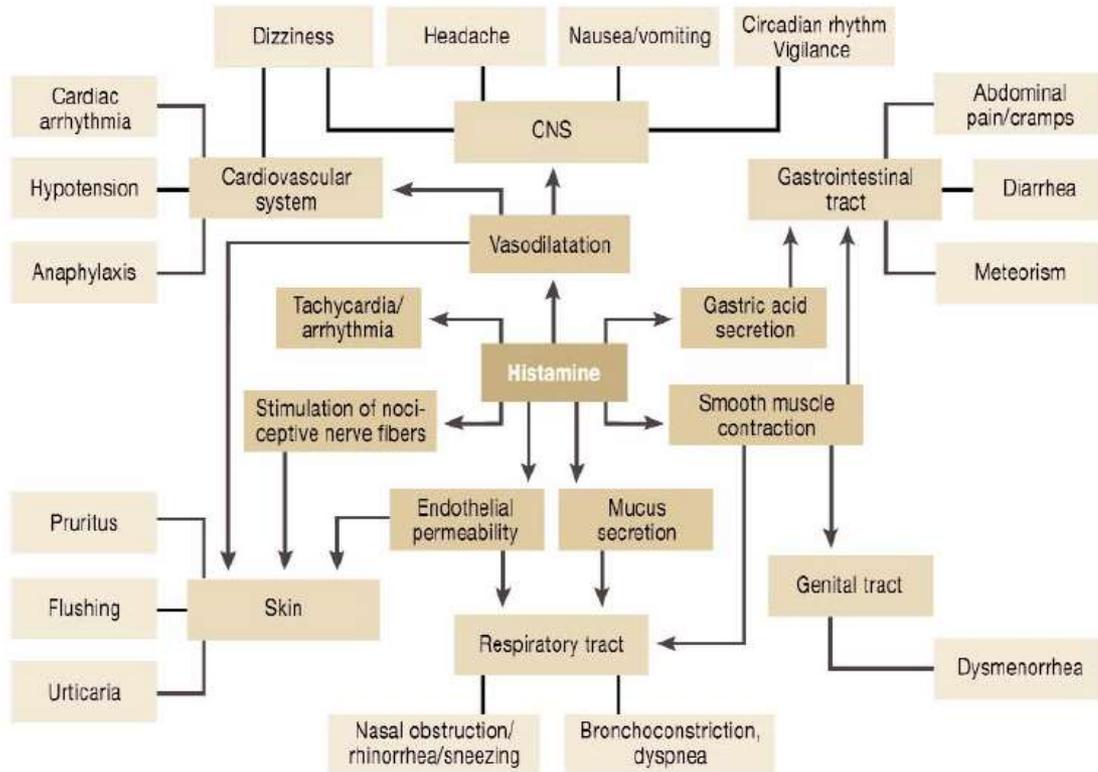
MEDICINE

REVIEW ARTICLE

Histamine Intolerance in Clinical Practice

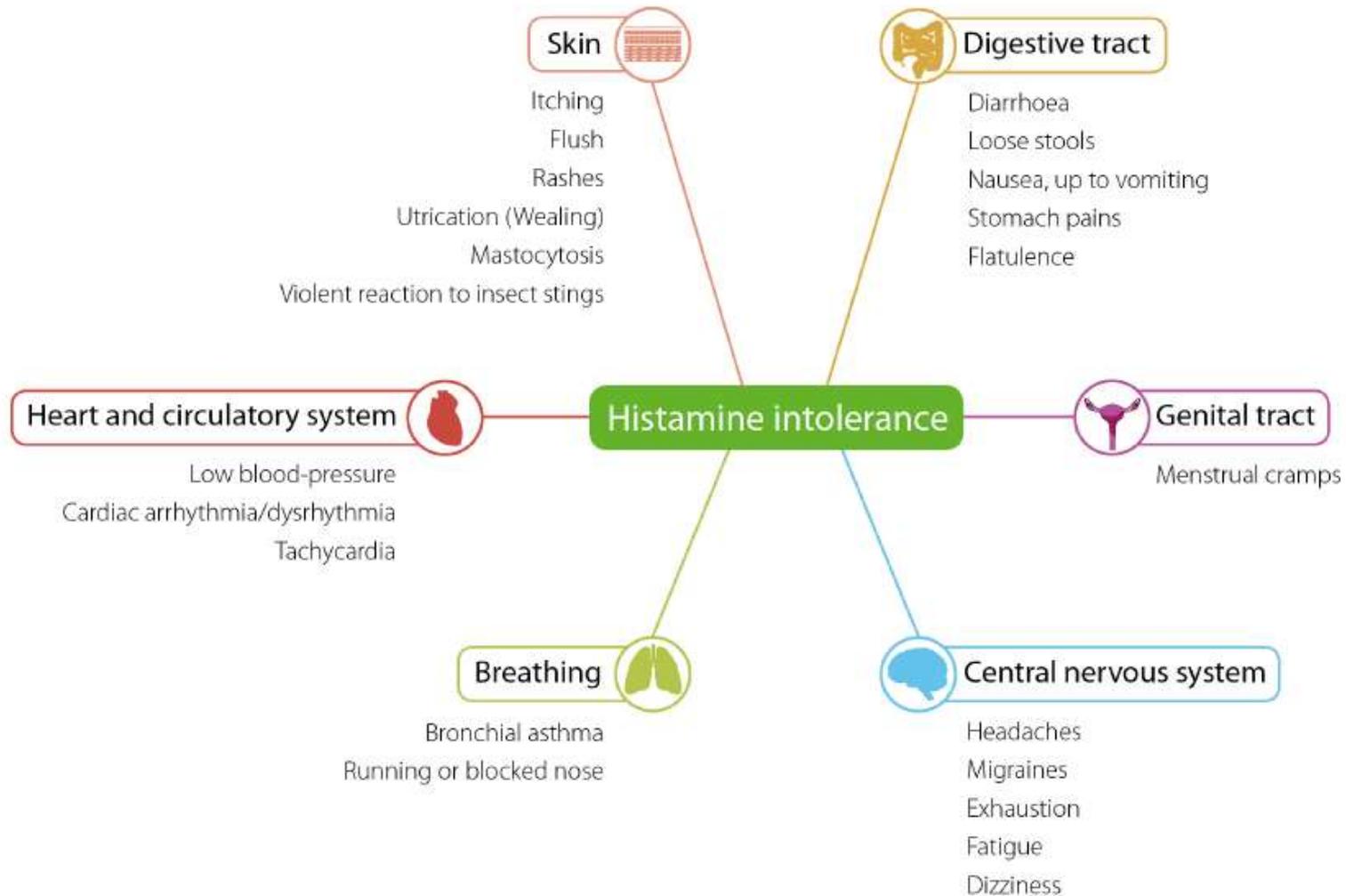
Laura Meintz, Thomas Bieber, Natalija Novak

DIAGRAM 2



“Inadequate histamine degradation based on a reduced DAO activity and the consecutive excess of histamine may cause numerous symptoms in multiple organs such as **diarrhoea, headache, hypotension, arrhythmias, urticaria, pruritus, flushing and even asthma** after ingestion of histamine-rich food, alcohol or drugs releasing histamine or blocking DAO. The multifaceted presentation means that **the condition is frequently missed.**”

Histamine intolerance a potential culprit across many body systems



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- Immune vs. non-immune-mediated food hypersensitivity
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 - Exclusion
 - Provocation
 - Stabilisation

Tailored recipes based around the results

BREAKFAST

Martina Musterfrau ■ date of birth: 12.07.1994 ■ sample id: 333333



AMARANTH PASTE

Ingredients for 2 servings

350 ml **water**
160 g **amaranth**

Directions

Add the amaranth to the boiling water and let soak on low heat for 25 minutes.

Proteins	Carbohydrates	Bread units	Fats	Energy
1,2 g	46,4 g	3,9	7,0 g	280 Kcal 1172 KJ

QUINOA-MILLET-WAFFLES

Ingredients for 4 servings

200 g **quinoa**
400 g **millet**
water
7 ml **oil (depending on tolerance)**
salt

Directions

Mix the cooked quinoa and the ground millet with water into a liquid dough. Add a dash of salt and 1 spoon of oil. Bake in the wafer iron at high temperature.

Proteins	Carbohydrates	Bread units	Fats	Energy
16,5 g	94,4 g	7,9	8,6 g	553 Kcal 2313 KJ

SOUPS

Martina Musterfrau ■ date of birth: 12.07.1994 ■ sample id: 333333



CARROT STEW

Ingredients for 4 servings

800 g **beef leg**
750 ml **yeast free vegetable broth**
500 g **baked potatoes**
1000 g **raw carrots**
salt
parsley, finely cut

Directions

Wash the crosscut shank and bring it to the boil together with the vegetable broth and a bit of salt in a large pot. Cook it for approx. 90 minutes at low heat.

Wash the carrots and peel the potatoes and cut them into equal bite-sized pieces. Add the vegetable to the shank crosscut and cook it all for another 20 minutes.

Take the crosscut shank out of the broth and remove the meat from the bone. Cut the meat into small pieces and put it back into the broth. Add the cut parsley to the soup and fill the soup in plates.

Proteins	Carbohydrates	Bread units	Fats	Energy
35,9 g	38 g	2,8	15,1 g	401 Kcal 1629 KJ

CHICKEN SOUP WITH VEGETABLES AND RICE

Ingredients for 2 servings

200 g **raw hen**
1000 ml **yeast free vegetable broth**
60 g **natural rice**
200 g **raw cauliflower**
300 g **raw leek**
400 g **raw carrots**
salt
spices and herbs (depending on the tolerance)

Directions

Wash and dry the chicken, salt and bring to boil. Cover and let simmer for 20 minutes.

Meanwhile, wash, clean and cut the vegetables into small cubes.

Add the rice and continue boiling for 10 minutes. Add the carrots and the cauliflower, after 5 minutes the leek and simmer everything for 15-20 minutes.

Take the chicken out of the soup, peel and break loose the meat of the bones. Cut the meat into small cubes and add to the soup. Add the chopped parsley and oil.

Proteins	Carbohydrates	Bread units	Fats	Energy

Recipes adapted to the exclusion criteria



HOME RECIPE ATTRIBUTES RECIPES BLOG PORTFOLIO

Topics	Seasons	Properties
BREAKFAST	SPRING	EGG FREE
BREADS	SUMMER	FISH
SWEET & SALTY SPREADS	AUTUMN	MEAT
SOUPS	WINTER	GLUTEN FREE
SALADS & DRESSINGS	CHRISTMAS	YEAST FREE
LUNCH & DINNER		LOW HISTAMINE
SIDE DISHES		COW'S MILK FREE
SWEETS		LOW CARB
SNACKS		WITH ALCOHOL
FOR IN-BETWEEN		NUT FREE
SMOOTHIES & DRINKS		WITHOUT HISTAMINE
FOOD 4 KIDS		WITHOUT INDUSTRIAL SUGAR
ICEAGE		OMEGA 3 SOURCE
		PROTEIN SOURCE

HOME RECIPE ATTRIBUTES RECIPES BLOG PORTFOLIO

HOW DO TO SUBSTITUTE INGREDIENTS AND WHERE TO BUY THEM (1)

HOW DO TO SUBSTITUTE INGREDIENTS AND WHERE TO BUY THEM (1)

FRUIT - PORRIDGE CHARGED WITH LOTS OF ENERGY

BUCKWHEAT PORRIDGE WITH FRESH FRUITS AND ROASTED BUCKWHEAT SEEDS

CARAMEL-CHIA PUDDING WITH FRESH BERRIES

HOME RECIPE ATTRIBUTES RECIPES BLOG PORTFOLIO

HOW DO TO SUBSTITUTE INGREDIENTS AND WHERE TO BUY THEM (1)

HOW DO TO SUBSTITUTE INGREDIENTS AND WHERE TO BUY THEM (1)

LIGHT, ASIAN MUSHROOM SALAD WITH A JUICY, PAN FRIED CHICKEN BREAST

ASPARAGUS SALAD WITH HERBS & ROASTED NUTS

A COLORFUL WILD-RICE POWER SALAD WITH ROASTED NUTS

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 - **Provocation**
 - **Stabilisation**

Three phases: Elimination, Provocation, Stabilisation

2.5 Summary

2 Provocation Phase

Avoided foods

- 1-day reintroduction
- 3-day observation

Allowed foods

- rotation

phase 1
**Elimination
Rotation**

phase 2
**Provocation
Rotation**

phase 3
**Avoidance
Rotation**

1 Elimination Phase

Foods to avoid

- strict 5-8 week elimination

Allowed foods

- 4-day rotation

3 Stabilisation Phase

Trigger foods

- 1-year avoidance

Allowed foods

- rotation

1. Elimination of the orange- and red-flagged foods

The foods with elevated and highly elevated values of IgG antibodies are strictly avoided during this phase. The initial elimination phase takes five to eight weeks. Please consult your health professional, a qualified dietician or nutritional expert to define the timeframe in your individual case.

Important: The level of IgG reflects the amount of IgG in your blood. Whether the IgG detected is relevant for a symptom or not does not depend on the amount of IgG. Even low levels of IgG to a food might cause severe symptoms, while high levels of IgG might not be responsible for a symptom. This means that elevated levels of IgG are as important as highly elevated levels.

By strictly avoiding the IgG positive foods, inflammation processes could be reduced or even stopped. This is an important preparation for the following provocation phase.



Practical tips:

- Read all labels on foods to make sure that you know what you are eating. Some foods can hide behind alternative names or can be contained in processed foods. Eggs, for instance, are used in many processed foods, such as cakes, meringues, ice cream or mayonnaise. They can be found under ingredient names like albumin, lysozyme, ovalbumin or ovoglobulin. Remember to check medications, beauty products, household products and your environment as well.
- Try to choose unprocessed foods whenever possible. There are a lot of additives in processed foods.
- Avoid products derived from IgG reactive foods. For example, if you have a reaction to cereals and yeast, also avoid beer. If you have a problem with grapes, then avoid wine, grape juice and raisins. The same applies to oils.
- Avoid the problem foods as strictly as possible. Your wellbeing will depend on your compliance during the elimination phase.

Note: At the beginning of the change in diet you might feel worse than before. This deterioration in how you feel can actually be a good sign. It could be due to your body detoxing. Drink plenty of fluids to help the process and keep to your new plan. Once the body has rid itself of any harmful substances, you will feel much better for it. The longest amount of time that this should last for is ten days. If the deterioration in your condition is extreme or goes on for longer than ten days, please consult your doctor.

Within the Elimination Phase: Rotation

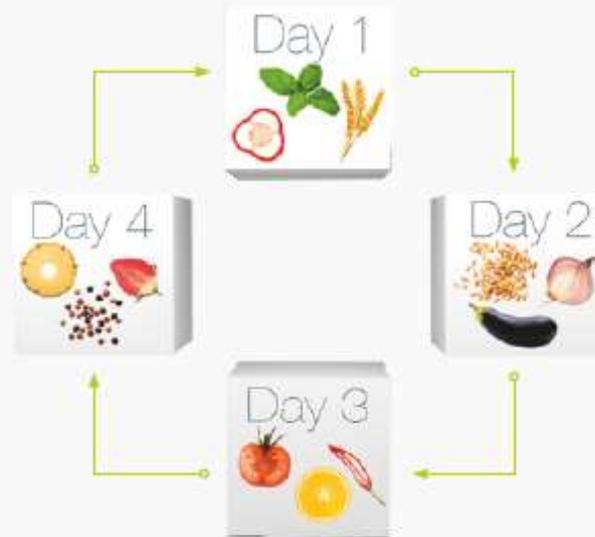
As we briefly explained to you already, the elimination phase consists of two parts: the rotation and the elimination.

The goal is to prepare your body for the following provocation phase by helping it to recover from IgG mediated inflammations in your body.

All the foods you are allowed to eat can be used to create your individual diet in a four-day cycle.

If you eat a certain selection of foods on the first day, you should avoid eating these for the next three days. This helps your body to heal from current IgG food allergies while reducing the possibility of forming new ones. It also ensures that you get all the vitamins and minerals you would expect from a varied diet.

Make up your individual "menu" of the allowed foods according to the 4-day rotation. It is up to you whether you plan your menu as you go or for the whole week. Just try it – you will soon find the most suitable approach for you.



"List 2 - Foods allowed and foods to avoid" shows you your personal selection of foods without elevated levels of IgG antibodies that can be eaten in rotation.

Personalised rotation schedules provided

Marina Musterfrau
 date of birth: 12.07.1994 / age: 28 / sex: f / sample id: 333333



List 3 - Rotation schedule

Tip: Build your individual rotation schedule

The rotation diet plan shown here is an example of how the rotation diet can be designed. You may like to choose your own selection of allowed foods for that day. What is most important is that each allowed food only appears once in the 4 day rotation plan.

	Day 1	Day 2	Day 3	Day 4
Cereals and starch				
	Amaranth	Arrowroot	Buckwheat	Carob
	Cassava	Fonio	Jerusalem artichoke	Maize, sweet corn
	Millet	Oats	Quinoa	Rice
	Sweet chestnut	Sweet potato	Tapioca	Teff
Meat				
	Beef	Chicken	Deer	Duck
	Goat	Goose	Hare	Lamb
	Ostrich	Pork	Quail	Rabbit
	Turkey	Veal	Venison	Wild boar
Milk products				
		Mare's milk		
Fruits				
	Apple	Apricot	Blackberry	Blueberry
	Cherry	Currant	Date	Fig
	Gooseberry	Grape / Raisin	Guava	Honeydew melon
	Lingonberry	Lychee	Mango	Nectarine
	Peach	Pear	Plum	Pomegranate
	Prickly pear	Quince	Rhubarb	Sea buckthorn
	Watermelon	Yellow plum		
Seeds and nuts				
	Coconut	Linseed	Pine nut	Poppy seeds
	Pumpkin seeds	Sunflower seed		
Salads				
	Butterhead lettuce	Dandelion	Endive	Iceberg lettuce
	Lamb's lettuce	Lollo rosso	Radicchio	Rocket
	Romaine / Cos lettuce			
Vegetables				
	Artichoke	Asparagus	Bamboo shoots	Beetroot
	Broad bean	Broccoli	Brussel sprouts	Carrots
	Cauliflower	Celeriac, knob celery	Chard, beet greens	Chickpeas
	Chili Cayenne	Chili Habanero	Chili Jalapeno	Courgette
	Cucumber	Green bean	Green pea	Kale, curled kale
	Kohlrabi	Leek	Lentil	Molokhia
	Mung bean	Okra, lady's finger	Olive	Onion
	Parsnip	Potato	Pumpkin	Radish (red/white)
	Rutabaga	Savoy cabbage	Soy bean	Stalk celery
	Sweet pepper			

2. Provocation Phase

2.2 Provocation Phase

Important: If you have an existing classic IgE allergy (type I) or any other known food intolerances, please do not start eating that particular food again. These foods must be excluded from the provocation phase.

Not all of the identified IgG reactive foods indicate the cause of certain symptoms. The provocation phase helps you to identify your personal trigger foods.

You now start your provocation diet and gradually reintroduce the previously eliminated foods one by one, with three days in between, back into your diet (see example on the following page). Start with the foods which are in the group "elevated" in your test results (orange). After completing the orange category, move on to the foods which are in the group "highly elevated" (red).

Note: You might find it easier to start the provocation phase with some of your favourite foods that were tested positive. This way, you will learn right away if your favourites cause symptoms or not. Please keep in mind that if these foods caused a reappearance of your symptoms you have to avoid them for at least one year. Afterwards you proceed with the foods from the category "elevated" as described above.

A trigger food may cause a specific symptom or lead to an increase in body weight. The increase of body weight is caused by the retention of water due to the inflammatory response to the food eaten. This food can lead to potential health risk in the future. Therefore, we recommend the following: If a reintroduced food causes returning symptoms or leads to an increase in body weight of approximately 1 kg or more overnight, then it must be left out of your diet for at least one year. If the food does not cause symptoms to return or an increase in body weight, it can be included in your diet again (we will come back to this when we talk about the stabilisation phase).



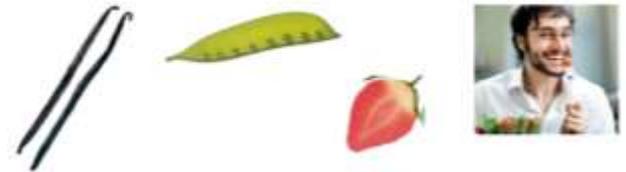
Guided provocation testing

Practical tips:

A provocation diary will help you to keep track of the reintroduced foods as well as the foods you need to avoid for one year. Just download the table and print it or make your own handwritten one. Below you will find an example of how to use the table.

- Start with the foods with elevated levels (orange).
- Pick one food from this category to include in a meal. Make sure that you eat a sufficient amount of the food and that it is the pure form of the food rather than a processed form, e.g. for hazelnuts you would start with the whole nut and not with a hazelnut cake. Note this food and the date of the reintroduction in the table.

- Note your health over the following three days and take your body weight daily. Do not reintroduce any new food yet.
- Have you had any adverse symptoms? Did any symptom that disappeared during the elimination phase reoccur? Did your body weight increase overnight as mentioned? If not, then you may continue to eat this food once a week. Fill in "No" in the columns "Symptom / increase in body weight" and "Avoid 1 year".
- If any symptoms have reappeared or new ones have developed, then you need to avoid this food for at least one year. Note the symptoms in the column "Symptom / increase in body weight" and fill in "Yes" in the column "Avoid 1 year". Then note the date one year from now in the column "Date of next provocation".
- Repeat these steps again for the other foods from this category with three days in between reintroductions. Then start on the foods with highly elevated levels (red).



Example "Provocation Diary"

Reintroduced food	Date of first provocation	Symptom / increase of body weight	Avoid 1 year	Date of next provocation
<i>Pineapple</i>	<i>01/09/2014</i>	<i>No</i>	<i>No</i>	<i>-</i>
<i>Milk (cow)</i>	<i>05/09/2014</i>	<i>Migraine 1.2 kg</i>	<i>Yes</i>	<i>05/09/2015</i>
<i>Vanilla</i>	<i>09/09/2014</i>	<i>No</i>	<i>No</i>	<i>-</i>

Provocation Diary				
Reintroduced food	Date of first provocation	Symptom / increase of body weight	Avoid 1 year	Date of next provocation

Note: You can download your individual provocation diary here:
<https://imupro.com/provocation-diary>

3. Stabilisation Phase

2.3 Stabilisation phase

The provocation phase helped you to find your personal **trigger foods**. During the stabilisation phase these foods are now avoided for at least one year, so that the IgG antibodies can be degraded and your body can recover.



The foods that do not cause any symptoms or gain in body weight overnight during the provocation phase may be reintroduced into your diet. This doesn't mean that it was a false positive result for this food. It means that this food does not induce a symptom yet, but still represents a potential threat to your health. To enable your body to eliminate IgG antibodies against this food we recommend eating it only once a week.

Note: If old symptoms or new symptoms appear during the stabilisation phase, one or more of the previously IgG positive foods could be the cause. In this case, repeat the elimination phase for five weeks for these foods. If your symptom disappears, one of the avoided foods is responsible for it. To identify the food(s), repeat the provocation phase with these foods, as described above. If your symptom does not disappear, either you have developed a reaction to a new food or food is not responsible for it. In this case we recommend consulting your therapist or physician.

After one year you can then start another provocation with the foods that you are still avoiding and reintroduce them one by one. You may find that there are one or two foods that you will even have to avoid permanently. If the food doesn't cause a return in symptoms or an increase in body weight after this second provocation, it can be included in your diet.

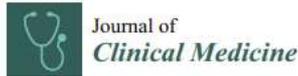
Practical tips:

- If you make a mistake, don't worry. An isolated incident won't set you back too much. You may feel a bit worse for a couple of days but continue to avoid all problem foods and you will get back to normal quickly.
- Try not to eat a food that was positive to IgG antibodies too often. If you manage to eat these foods only once a week you may tolerate them again.
- Make a habit of a varied diet to ensure that you get all the vitamins and minerals you need. By rotating the foods you may have less variety in one day but more variety over the week.
- Keep a record of your body weight, even if you don't have weight problems. An increase in body weight overnight of approximately 1 kg or more is an indication that you consumed a non-tolerated food the day before.
- If a new symptom which might be related to chronic inflammation occurs within or after 12 months and you still comply with your diet, then a new trigger food might be present. This could be an indication for a new ImuPro test.

Summary

1. **Elimination** based on the IgG test results. This phase is kept **very short, 5 weeks**, which should be sufficient to improve symptoms if related to IgG positive foods according the published studies.
2. After the 5 weeks, Phase 2 is started: the **provocation or challenge phase** (recognized as golden standard in allergy). Each food is reintroduced according to a strict procedure to evaluate which are the real individual trigger foods causing the symptoms. This will allow reintroduction of some of the foods previously avoided.
3. Phase 3 is the **real exclusion phase**, where all foods identified as trigger foods are avoided for one year. Integral to all three phases is the **rotation diet**, meaning the subject should not eat the same food within 4 days. A rotation diet ensures that a deficiency in micro- or macronutrients does not occur. In practice the diet is usually much more diversified than most subjects have ever experienced previously.

A large-scale study conducted using exactly the ImuPro test and strategy revealed impressive results



Article

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

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Abstract: Irritable bowel syndrome (IBS) is a chronic disease with recurrent abdominal pain, disturbed bowel emptying, and changes in stool consistency. We compared the effectiveness of three different dietary treatment plans (G1-FM-low FODMAP diet, G2-IP IgG based elimination-rotation-diet, and as control group, the G3-K control diet recommended by an attending gastroenterologist) in treating patients diagnosed with mixed irritable bowel syndrome. A total of seventy-three female patients diagnosed with a mixed form of irritable bowel syndrome (IBS-M) were enrolled in the study. The diet of each patient in Group 1 (G1-FM) and 2 (G2-IP) was determined individually during a meeting with a dietitian. Patients from Group 3 (G3-K) received nutrition advice from a gastroenterologist. Significant differences in the reduction of IBS symptoms were found between the groups. IBS symptoms as well as comorbid symptoms significantly improved or disappeared completely in the G2-IP group (idiopathic abdominal pain, $p < 0.001$; abdominal pain after a meal, $p < 0.001$; abdominal pain during defecation, $p = 0.008$), while in the G1-FM group, some of the IBS symptoms significantly improved (mucus in stool, $p = 0.031$; bloating, $p < 0.001$). In group G3-K 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 IBS-M patients do not uniformly affect the course and outcomes of disease management. Rotation diets based on IgG show significantly better results compared to other diets.



Citation: Ostrowska, L.; Wasiluk, D.; Lieners, C.F.J.; 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*, 4317. <https://doi.org/10.3390/jcm10194317>

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“This study shows that a personalized dietary approach is more effective in treating IBS-M than generalized 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 ... Rotation diets based on IgG show significantly better results compared to other diets.”

Numerous cases available



INFLAMMATORY DERMATOSES AND FOOD ALLERGIES IN CHILDREN: TO BE OR NOT TO BE?

Gabriela Ion, Raluca-Gabriela Miulescu, , Alexandra Voicu

Background

Currently, numerous inflammatory skin diseases have been described among pediatric patients, so there are also multiple treatment guidelines suitable for each individual case. Among the most common inflammatory skin diseases are: atopic dermatitis, psoriasis, eczema, or prurigo. Also, in the literature, rare skin pathologies are mentioned, such as Kawasaki disease or calcinosis cutis. It is known that these diseases are influenced by various trigger factors. The most discussed lately is the association between inflammatory skin conditions and food

Observations

In this case series, we present two pediatric patients with inflammatory skin diseases: numular eczema, atopic dermatitis and chronic prurigo. These patients did not respond to conventional therapy, so we investigated for other possible triggers. What these children had in common were gastrointestinal manifestations or other immune-mediated pathologies. Therefore, we reconsidered the mechanism of the disease, thinking what else can initiate an immune conflict. Because we suspected a type III Ig G food allergy, we performed a specific test, and also microbiota tests.

We excluded the foods involved from the diet and corrected the gut dysbiosis. On average, after 2 months from the start of this treatment, associated with dermatological therapy, the improvement was significant.

First, we present the case of a 6-years-old male patient, who referred to our clinic for persistent lesions of prurigo and eczema, non-responsive to conventional therapy (Figure 1).



Figure 1 – Chronic prurigo and eczema

We performed several laboratory tests, and identified: positive antitransglutaminase Ig A and Ig G antibodies; ImoPro test, for type III Ig G food antibodies showed several food allergies, but specifically to gluten, milk and eggs (Figure 2). Interdisciplinary management consisted in topical therapy (corticosteroids Advantan, emollients, calamine creams), as well as diet and treatment of dysbiosis.



Figure 2- Type III Ig G food allergies

Evolution was favorable, with remission of lesions in 6 weeks, and maintaining remission (Figure 3).



Fig. 3-Remission of lesions

The second case is about a male patient, aged 1 year-old, who referred to our clinic for atopic dermatitis, with exudative lesions (Figure 4).



Figure 4- Atopic dermatitis

We performed ImuPro test, and identified multiple delayed food allergies, especially dairy. (Figure 5).



Management consisted in local treatment (Fucicort, Emollients), diet and specific probiotics. Evolution was favorable, with complete remission of eruption.

Key message

Virtually, any leaky gut trigger can initiate an immune conflict. Inflammatory dermatoses are often associated with delayed food allergies. What type of hypersensitivity or what organ is involved depends on the genetics of the patient.

Chronic eczema and food intolerances in paediatric patients: cases from the European Academy of Dermatology and Venereology

Chronic eczema and food intolerances in pediatric patients

Gabriela Ion, Raluca-Gabriela Miulescu

Introduction

Chronic eczema is an inflammatory disorder, triggered by different factors. Usually, in children, a possible role is represented by an infectious disease, acute or chronic. On the other hand, we should consider other inflammatory or immune-mediated disorders, if the lesions persist or do not respond to conventional therapy. In this paper, we focused on the mechanism of the disease, the immunological damage, and the possible cross-reactions between gliadin and tissue antigens.

Materials and methods

We present a case of a 14-year-old female patient, known with recurrent eczema, diagnosed 1 year ago, who referred to our clinic for management of the disease (Fig. 1, 2). She was



Fig. 2: Initial lesions

Results

New theories about inflammatory diseases in children are based on different food allergies, as mentioned before (Fig.3). So, we performed a genetic celiac disease test, as well as specific antibodies. Genetic test was positive, but the antibodies were negative. We also tested our patient for Ig G mediated food allergies; the child already

Fig. 4: Type III food allergies



Recurrent guttate psoriasis and celiac disease in childhood: cases from the European Society for Pediatric Dermatology

Recurrent guttate psoriasis and celiac disease in childhood: an association to be considered

Gabriela Ion, Raluca-Gabriela Miulescu, Elena Alexandra Voicu, Georgiana Laura Bosneag

Objectives

Guttate psoriasis is a chronic, inflammatory disorder, triggered by different factors. Usually, in children, a possible role is represented by an infectious disease, acute or chronic. On the other hand, we should consider other inflammatory or immune-mediated disorders, if the lesions persist or do not respond to conventional therapy. In this paper, we focused on the mechanism of the disease, the immunological damage, and the possible cross-reactions between gliadin and tissue antigens. (Fig. 1).



Fig. 2: Initial lesions



Fig. 3: initial lesions



Fig. 5: IgG type III allergies

Fig. 6: Type III food allergies

7-years-old female patient, known with guttate psoriasis, since the age of 4 years old, with multiple recurrences, who referred to our clinic for second opinion (Fig.2). We also present a case of a 14-years old female with the same cutaneous pathology (Fig.3). So, we reconsidered the mechanism of the disease, thinking what else can we do for a guttate psoriasis, which has not improved on conventional treatment. The suspicion of immunological damage is maintained, especially due to the association with guttate psoriasis and other autoimmune, inflammatory disorders.

gastrointestinal symptom. We recommended exclusion of gluten from the diet. Surprisingly, the evolution was favorable, with complete remission of the eruption and maintaining this course (Fig. 4). As for the second patient, she was diagnosed with multiple Ig type III food allergies (Fig. 5, 6). After diet, the evolution for good, as well.



Fig. 4: Remission

Discussion

Virtually, any leaky gut trigger can initiate an immune conflict. What type of hypersensitivity or what organ is involved depends on the genetics of the patient. The path of recovery is the same of that of disease, but in reverse. Healing means helping the immune system do what it needs to do according to the information in the DNAd.

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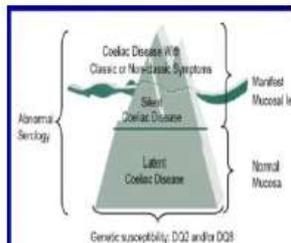


Fig. 1: Subtypes of celiac disease

Results

New theories about inflammatory diseases in children are based on different food allergies, as mentioned before. So, we performed a genetic celiac disease test, as well as specific antibodies. As we expected, the test and the antibodies were positive. So, we were able to diagnose celiac disease, even in the absence of

Method

We present a case of a



European Society for Pediatric Dermatology

References: B. Admou et al, "Atypical Celiac Disease: From Recognizing to Managing", *Gastroenterology Research and Practice*, vol. 2012, Article ID 637187, 9 pages, 2012. <https://doi.org/10.1155/2012/637187>

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- ImuPro tests for IgG 1 - 4 antibodies. Many other widely available food sensitivity tests just test for IgG 4, which could result in a false negative result for a patient.
- ImuPro can test for reactions against up to 270 potential antigens.
- Most antigens in the ImuPro test are foods, but also included are *Candida Albicans* yeast and *aspergillus niger*, a mould that grows on some grains during storage. This can highlight a separate reason for intolerance to certain grains that would not otherwise show up in tests for the specific foods only.
- The food proteins used in the test are organic. This avoids potential cross-reactivity with pesticides, fungicides and herbicides that could occur with sensitivity tests that use conventionally-farmed foods for testing.
- Detailed test results show the strength of the immune system reaction to a food, graded from weak to strong, allowing you to prioritise food elimination with your patient to improve compliance.
- Depending on the level of test chosen, they can be accompanied by a personalised food rotation plan and an optional recipe book for your patient, all of which exclude foods that ImuPro has revealed as causing intolerances. You can also choose to exclude other foods from these, regardless of the ImuPro findings - for example, due to previous diagnoses such as a food allergy (IgE mediated).

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Thanks very much for your attention!
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