Food-Specific IgG Titers as a Dietary Guide in Food Intolerance

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Chronic unspecific symptoms such as diarrhoea, constipation, bloating, nausea, migraine, asthma, eczema, arthritis or fatigue can have many different causes, including reactions to ingested food. It is often difficult to pinpoint the trigger of such symptoms and applying a routine exclusion diet is not always useful due to widely differing patient responses. Testing for antibodies of class IgG against different foods and food additives may help to establish if an immune-mediated food intolerance is behind the health problems. If high concentrations of IgG antibodies against a particular food are identified, elimination of the offending substance from the diet may help to relieve symptoms. Thus, a comprehensive IgG analysis can help to tailor an individualised approach to diet management.

Food Intolerance

Food intolerance or food hypersensitivity is a detrimental reaction to a food or food additive. It may be caused by enzyme defects (e.g. lactose or histamine intolerance), food pharmacologicals (e.g. glutamate, sulphites, vasoactive amines, additives), toxins (e.g. aflatoxins) or IgG-mediated immune reactions.

Food intolerance differs from immediate-type, IgE-mediated food allergy (type 1 allergy) in that reactions are typically delayed and symptoms tend to be more generalised and chronic. In a classic IgE-mediated allergic reaction, consumption of an offending food results in a rapid release of histamine and immediate symptoms of tingling mouth, hives and swelling of the lips, face, tongue and throat. Severe allergic reactions (anaphylaxis) can lead to acute breathing problems and low blood pressure and can be life-threatening. In IgG-mediated food intolerance, on the other hand, onset of symptoms ranges from several hours to days after intake of the food. The most frequent symptoms are diarrhoea, constipation, bloating, nausea, upset stomach, irritable colon, migraine, asthma, joint disorders, lack of concentration, skin disorders and weight gain or loss.

The mechanisms of IgG-mediated food intolerance are immune-complex based. Partially digested food components pass into the bloodstream, inducing the production of IgG antibodies and the formation of antigen-antibody complexes. If the immune complexes are not sufficiently cleared, they are deposited in tissues, causing inflammation. Patients with a compromised immune system or an increased permeability of the intestinal wall, so-called leaky gut syndrome, are particularly susceptible to these inflammatory reactions. A leaky gut can be caused by diet-related hyperacidity of the gut flora, medication, infections, preservatives, alcohol, nicotine or stress or further factors. The immune complexes are preferentially deposited in tissue that is already damaged or inflamed due to e.g. disease, infection or environmental toxins, resulting in augmentation of the inflammation and chronic symptoms.
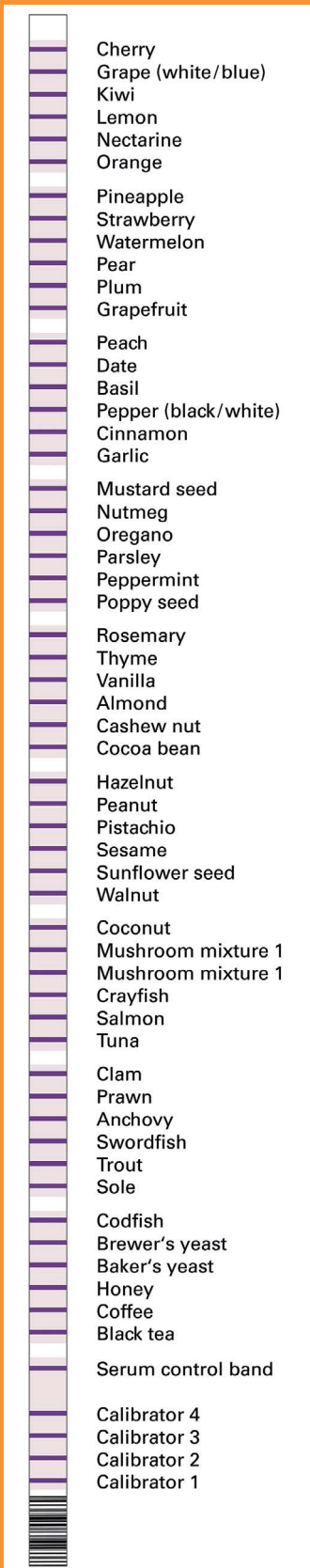
To relieve symptoms, an elimination diet for a set period of time is usually recommended. The foods for which high IgG antibody concentrations were measured are excluded from the patient's diet. Improving the gut flora by therapeutic measures can also be considered to reduce or prevent the permeability of the intestinal wall to food antigens.

IgG Subclasses

IgG antibodies have various functions, such as neutralisation of antigens, activation of the complement cascade, flagging of antigens for destruction (oponisation) and phagocyte binding. However, the four different subclasses of IgG play different roles (Table 1). Due to their strong oponisation and complement activation properties, IgG_1 and IgG_3 and to a lesser extent IgG_2 are pro-inflammatory. IgG_4 on the other hand has protective, anti-inflammatory properties. IgG_4 plays a defensive role in type I allergy, acting as an antagonist of IgE. It induces the release of histamine, although to a much lesser extent than IgE. Therefore, IgG_4 antibodies may lead to allergy symptoms particularly in histamine-intolerant patients. However, in chronic inflammatory processes, only the subclasses IgG_1, IgG_2 and IgG_3 are relevant. Since IgG_4 antibodies make up only a small proportion of all IgG, testing for total IgG is sufficient to detect clinical relevant titers of pro-inflammatory IgG_1, IgG_2, and IgG_3 antibodies. ▶

Testing for antibodies of class IgG against different foods and food additives may help to establish if an immune-mediated food intolerance is behind the health problems.

Cherry
Grape (white/blue)
Kiwi
Lemon
Nectarine
Orange

Pineapple
Strawberry
Watermelon
Pear
Plum
Grapefruit

Peach
Date
Basil
Pepper (black/white)
Cinnamon
Garlic

Mustard seed
Nutmeg
Oregano
Parsley
Peppermint
Poppy seed

Rosemary
Thyme
Vanilla
Almond
Cashew nut
Cocoa bean

Hazelnut
Peanut
Pistachio
Sesame
Sunflower seed
Walnut

Coconut
Mushroom mixture 1
Mushroom mixture 1
Crayfish
Salmon
Tuna

Clam
Prawn
Anchovy
Swordfish
Trout
Sole

Codfish
Brewer's yeast
Baker's yeast
Honey
Coffee
Black tea

Serum control band

Calibrator 4
Calibrator 3
Calibrator 2
Calibrator 1

Headaches and Migraine

Migraines have a complex etiology, but it is known that food can play a role in inducing or aggravating attacks. Already in the 1930s the benefits of an elimination diet were demonstrated. In recent studies, elimination diets based on IgG levels have been shown to have significant positive effects, such as reduction of the number of headache days, attack count or duration and severity of migraines. A further study revealed significant differences in the number of positive results for IgG to foods between 56 migraine sufferers and 56 controls, and elimination diets successfully controlled the migraines of these patients without the need for medication.

Arthritis

Food intolerance has been known for many decades to be a causative factor for developing arthritis. In a study of 22 patients with rheumatoid arthritis undertaking an elimination diet, 91% experienced an improvement of symptoms. All but one of these patients suffered a deterioration of their health status when the reactive foods were reintroduced into their diet.

Irritable Bowel Syndrome

Irritable bowel syndrome (IBS) is the most common functional gastrointestinal disorder with a reported prevalence in the general population of 12 to 22%. The disease is poorly understood, but food intolerance is a major factor in its pathogenesis. Specific foods can provoke symptoms of IBS, while patients treated with dietary exclusion frequently show symptomatic improvement. In a study on 150 IBS patients, an elimination diet based on raised IgG antibodies resulted in a 26% improvement in the symptom score compared to a sham diet, while relaxation of the diet led to a 24% deterioration. In a further study, 20 IBS patients showed significant improvement after food elimination and rotation diet based on serum IgG measurements.

Inflammatory Bowel Diseases

A retrospective study on 112 patients with inflammatory bowel diseases (IBD) (79 with Crohn's disease and 33 with ulcerative colitis) and 266 healthy individuals showed that patients with inflammatory bowel diseases exhibit a high prevalence of antibodies of class IgG against certain foods and that

this can be used to establish an elimination diet. Further studies have similarly shown higher levels of food IgG antibodies (e.g. against yeast and processed cheese) in Crohn's patients than in healthy controls, and demonstrated that nutritional intervention based on circulating IgG antibodies against food antigens can improve symptoms.

Asthma and Atopic Dermatitis

Increased levels of IgG antibodies against foods or food additives have also been observed in asthma and atopic dermatitis. For example, in 125 patients with beef allergy manifesting with asthma, dermatitis or gastrointestinal disorders, beef-specific IgG and also IgA were significantly detected alongside and sometimes in the absence of specific IgE. An elimination diet ameliorated the symptoms in all of the allergic patients. In another study, significantly elevated levels of IgE and IgG were found in a relatively high proportion of patients with atopic dermatitis compared to controls.

Autism

The etiology of autism is not well understood, but dietary restrictions are beneficial and a prerequisite to benefit from other interventions. The main foods for exclusion are milk and dairy products, wheat and other gluten sources, sugar, chocolate, preservatives and food colouring. Individualised IgG and IgE testing can identify other troublesome foods. In a study of 36 infantile autistic patients, high levels of antibodies including IgG against milk proteins were found compared to control children. Behavioural symptoms improved on an elimination diet, indicating a possible relationship between food allergy and autism.

Diagnostic Value of IgG Testing

The diagnostic value of IgG antibody detection for the diagnosis of food intolerance is controversially discussed. Nevertheless, different studies with up to several thousand patient samples have come to the conclusion that the determination of the antibody titer can be a useful tool for the identification of food intolerances and for targeted patient therapy. Generally, it could be shown that elimination of those foods against which strong antibody reactions were measured helped to improve symptoms or to promote complete recovery in a statistically significant number of patients. A large internet-based study on the diagnostic benefit and clinical

relevance of IgG antibodies as a marker of food intolerance concluded that IgG determination provides a clinically useful basis for establishing an elimination diet.

IgG Determination

IgG antibodies against different food and food additives can be easily determined by immunoassay. Immunoblots are particular useful for this application as they allow multiparameter analysis of hundreds of different parameters in parallel, providing an extremely wide-ranging screening (Figure 1). This is especially important in food intolerance, as symptoms tend to be delayed or chronic and may be difficult to link with consumption of a particular food.

Total IgG against 108 or 216 foods and food additives can be analysed simultaneously with a new range of immunoblot profiles based on established EUROLINE technology. The foods represented on the strips are divided into categories, encompassing gluten-containing cereals, gluten-free cereals and alternative foods, meats, dairy and egg, fruits, herbs and spices, nuts and seeds, vegetables, legumes, salads, mushrooms, fish and seafood, and other foodstuffs such as yeasts, honey, coffee

and black tea. Only small volumes of patient serum are required for the analysis, just 40 µl for 108 results. By analysing 22 patient samples in one run, 2,376 single results can be obtained in just 4.5 hours. Results are evaluated semiquantitatively using four calibrators corresponding to the WHO reference serum 1st IRP 67/86. To increase productivity further the entire procedure, from sample identification and incubation to evaluation and archiving of results, can be fully automated e.g. on the EUROBlotOne device with EUROLineScan software.

Perspectives

The determination of IgG antibodies against food and food additives can contribute to the diagnostic workup for patients with chronic

food-related health problems. Although the link between food-specific IgG antibodies and chronic inflammatory processes has not yet been firmly established, many studies have demonstrated an association between food IgG antibodies and different diseases, and shown that elimination diets based on IgG reactions can help to relieve symptoms. Thus, patients with unspecific gastrointestinal and other symptoms which cannot be attributed to any known cause may benefit from a comprehensive IgG analysis and a corresponding elimination diet. As with classic IgE allergy tests, IgG results should always be interpreted in the context of clinical observations. Further studies should help to clarify the role of food-specific IgG antibodies in poor gut health. ML

▼TABLE 1: Properties and abundance of different IgG subclasses				
	IgG_1	IgG_2	IgG_3	IgG_4
Property				
Neutralisation	++	++	++	++
Oponisation	+++	+	++	-
Complement activation	++	+	+++	-
Medium serum concentration (mg/ml)	9	3	1	0.5
Abundance	66%	23%	7%	4%