

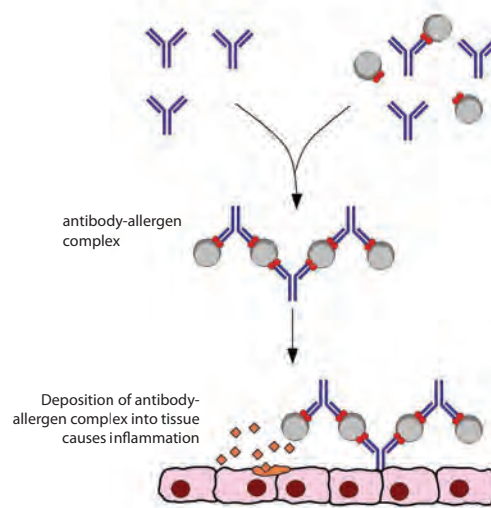
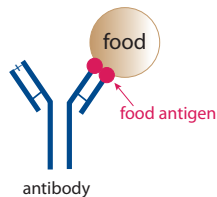
IgG Type III Delayed Hypersensitivity Reactions

Circulating IgG antibodies form an immune complex with an allergen/antigen (Ag). This is considered a Type III delayed hypersensitivity reaction, and typically occurs over several hours to several days.

Formation of the complex activates the complement pathway and releases inflammatory mediators.

The IgG-Ag immune complexes are usually cleared by macrophages but, in the presence of excess antigen, macrophages may saturate their capacity to remove immune complexes, causing the excess to be deposited in tissue. Deposition of IgG-Ag complexes causes inflammation and tissue damage, which may contribute to specific health issues.

There are four subclasses of IgG: IgG1, IgG2, IgG3 and IgG4. All subclasses activate the classical complement pathway except for IgG4. Our IgG test measures all four subclasses, and reports the result as total IgG.



Clinical Relevance

Although still controversial in mainstream medicine, IgG food sensitivity testing is starting to accumulate research in support of its clinical utility. For example, 125 patients, identified by an allergist as likely having food allergies, were given blood tests for IgG food reactions. All positive foods were removed for a 6 month period. The allergist considered the treatment a success when a minimum 75% improvement in symptoms occurred. Of the 80 patients who completed the full course, 71% were successfully treated. In particular, there were 11 patients who had positive allergy symptoms, but had negative IgE test results. These patients were all successfully treated by eliminating the IgG food allergens. The allergist concluded that blood tests for IgG reactions to food were clinically useful and much more palatable to patients than the traditional skin prick and oral challenge tests.

Although he acknowledged that the lack of blinding and randomization meant the results could be considered anecdotal, the allergist concluded that eliminating reactive foods was useful clinically. [Otolaryngol Head Neck Surg. 2000;123(1 Pt 1):48-54].

IgG testing for food is not considered diagnostic for food reactions because a direct cause-effect relationship has not been firmly established. In other words, elevated levels of IgG have not yet been proven to cause patient symptoms. However, more and more studies are emerging to show a correlation between elevated IgG reactions and a variety of conditions.



IgG Food Sensitivity

IgG delayed onset reactions can contribute to a variety of health problems.



Conditions Related to Elevated IgG Levels

Irritable Bowel Syndrome

A double-blind 2004 British study randomized 150 patients to receive either a sham diet or true diet. The true diet group eliminated all IgG reactive foods, and the sham diet group excluded the same number of foods as showed up reactive, but not the actual foods. The severity of IBS symptoms, non-IBS related symptoms, anxiety/depression and quality of life scores were obtained at the start and again after three months on either diet. At the end of the study, the true diet group had significantly reduced severity of IBS symptoms and overall symptoms compared to the sham diet group. [Gut. 2004 Oct;53(10):1459-6]

Migraine

A 2004 study looked at the relationship between IgG food reactions and migraine attacks. In the study, 61 people were tested via IgG ELISA for 113 foods. About 90% of participants eliminated some or all of the reactive foods from their diet. At 1 month, 30% reported marked improvement, and at 2 months 40% reported benefit. Reintroduction of the reactive foods into the diet resulted in return of migraine for 60% of these patients. This study suggests that IgG reactions to food may play a role in the etiology and/or treatment of migraine attacks. [Headache Care. 2004; 2(1):11-14]

A 2010 randomized, double-blind, crossover trial also showed a statistically significant drop in the number of headache days, and the number of headaches during the six weeks IgG reactive foods were eliminated from the diet. [Cephalalgia. 2010;30(7):829-37]

Weight Gain / Atherosclerosis

A paper published in 2008 reported that obese children have significantly higher IgG antibodies to food antigens than normal weight children. They also found that anti-food IgG antibody concentrations are strongly associated with low grade systemic inflammation and with increased intima media thickness of the common carotid arteries. The study concluded that: "These findings raise the possibility that anti-food IgG is pathogenically involved in the development of obesity and atherosclerosis." [Exp Clin Endocrinol Diabetes. 2008; 116: 241-45]

Atopy

Allergic individuals and those with atopy achieved 70% reduction of symptoms with elimination of IgG reactive foods. [Ann Allergy. 1987 Nov;59(5 Pt 2):137-40] In addition, atopic children (with or without eczema) were shown to have higher IgG levels to specific foods than non-atopic children. In children without eczema, higher levels of IgG were still significantly associated with atopy, with elevated IgG most prominent to egg white, orange and cow's milk. [Clin Exp Allergy. 1999 May;29(5):604-10]

Rheumatoid Arthritis

Some rheumatoid arthritis patients have shown improvement in symptoms when reactive foods were eliminated from the diet. It has been hypothesized that patients with occasional rheumatitis may experience delayed hypersensitivity food reactions. [Food Allergy. 1997. American Academy of Otolaryngic Allergy]

ADHD

Although no studies directly correlate elevated IgG levels to specific food with hyperactivity in children, a few studies have shown improvement in child attentiveness and temperament when common food allergens (e.g. wheat, dairy, oranges) were eliminated.

About IgG Testing for Food Sensitivity

Procedure: The IgG blood spot measures levels of IgG antibodies to 96 different foods. Antibodies are highly specialized protein molecules that bind to specific antigens. All foods have antigen molecules on them, and sometimes these food antigens can trigger the production of antibodies. The exact reason why food antigens trigger the release of IgG antibodies is not known.

Antibody levels are measured via an ELISA (Enzyme Linked Immunosorbent Assay) method. For an ELISA test, food antigens must first be chemically bonded to the surface of a tray containing multiple wells. Each of these wells is coated with the food antigens of one specific food. Up to 96 foods can be tested on a single tray for any given patient. Measured amounts of the patient's blood are placed in each well and then the entire tray is treated with a series of chemical solutions. Eventually a colour develops in each well, and the intensity of the color is measured by a spectrophotometer. The degree of colour change reflects the amount of antibody in the blood specific to the food present in that well. The colour for each food is compared to known standards to determine how much of a reaction has taken place.

Source of Food Antigens: Foods are sourced from major North American grocery warehouses (regulated by USDA or FDA) and are assayed for total protein content. Quality control procedures ensure the protein source is correct and that no other contaminants are present. Proteins are de-fatted, freeze-dried (lyophilized), stoppered under vacuum and stored at less than 0°C (the lyophilization process involves the drying of the food source by freezing it and then subliming the remaining product in a high vacuum). Lot-to-lot analyses are done both by the manufacturer and in-laboratory upon receipt.

Accuracy: There is no accepted standard for determining accuracy of an IgG food sensitivity test, although interlaboratory comparisons are completed twice yearly. In general, multiple analyses of the same sample/same patient are the best means for ascertaining reliability of a test. A study published in Natural Medicine Journal compared the IgG food sensitivity blood strip test offered exclusively through Rocky Mountain Analytical to a cell size variability method. Results showed that on repeat testing, 99% of the IgG foods tested were within one reactivity level of one another (82% were in the same level). For the cell size variability method, repeat testing found that only 14% of foods were within one reactivity level of one another (only 2% within the same level).

Similarly, a Swedish health website compared five laboratories that perform IgG food sensitivity testing. Only one of the five laboratories tested had reproducible results (as determined by testing two samples from one patient), and that was the IgG blood spot test offered exclusively through Rocky Mountain Analytical. [http://www.usbiotek.com/news_swedish_analysis.php]

Regardless of the laboratory or testing method used, false negative or false positive results may occur.

False Positives / False Negatives

False Positives

- **Cross-reactivity:** False positives may occur as a result of cross-reactivity with other foods or proteins. This can occur when the proteins are not identical, but similar enough that the immune system reacts to them. For example, a reaction to bananas may also produce a reaction to latex or vice versa.

There is an antibody pattern (either IgE or IgG) seen in a small subpopulation that has elevated antibodies to vegetables, fruits and grains. In these individuals, the high antibody levels to plant glycoproteins do not appear to be clinically relevant. Nevertheless, the practitioner must use his/her professional judgement to ascertain the significance of the results relative to the patient's clinical picture. [Allergy. 1998 ;53(S 46):58-61]

- **Leaky Gut:** When the gut lining is inflamed, food particles can leak through and be considered foreign bodies. This can lead to elevated IgG levels for all the foods the patient normally eats. Leaky gut may originate with one or more food allergies, or may be a result of stress or prescription drug or alcohol consumption. [Alt Med Rev. 1997 ;2(5):330-45]

False Negatives

- **No Exposure:** If the allergen was not consumed in the 7 days prior to testing for IgG (or 24 to 48 hours for IgE) antibody levels *may* drop enough that no significant food reactions are apparent. However, there are no studies that demonstrate the precise impact of food avoidance on antibody levels, so individual variability in antibody level decline is likely. Ideally have the patient consume a regular-sized serving of the food at least twice a week for two or three weeks prior to testing. [Food Allergy. 1997. Thieme Medical Publishing]. Foods that are not consumed regularly may or may not give accurate results.
- **Alteration:** The form of allergen being tested is not the same as what the patient reacts to. For example, whey protein is altered by high heat, so someone with a whey allergy may have no reaction to heat-altered milk products. Or, raw eggs show no reaction, but cooked eggs may be a problem.
- **Non-Immune:** Enzyme deficiencies, toxins and chemicals found in foods may mimic the symptoms of a food allergy but are not the result of an immune reaction. See chart on next page.

Non Immune Mediated Reactions

	Implicated Substance	Associated Foods	Possible Symptoms
Enzymes	lactase deficiency	lactose in dairy products	nausea, diarrhea, gas, bloating, and abdominal cramps
	alpha-galactosidase insufficiency	cruciferous vegetables, legumes	gas, bloating
Chemicals	histamine	fish, sauerkraut, cheese	headaches, rashes, itching, diarrhea, vomiting and/or abdominal pain
	methylxanthine	cola, coffee, chocolate, tea	anxiety, panic disorders
	tyramine	cheese, pickled herring	headache, palpitations, nausea, vomiting
	tryptamine	fermented foods (soy sauce), Acacia species (incl. beans)	restlessness, agitation, gastrointestinal distress, muscle tension, may be hallucinogenic
Toxins	aflatoxin	peanuts, cereal grains	chronic exposure: liver disease, increased risk of liver cancer
	saxitoxin	shellfish	inhalation: numbness & tingling of lips, tongue, and fingertips, followed by numbness of the neck and extremities and motor incoordination. Other symptoms may include light-headedness, dizziness, weakness, confusion, memory loss, and headache
	ergot	cereal grains	numbness, tingling & burning in limbs, feeble pulse, restlessness, stupor, delirium
	cyanogenic glycosides	stone fruits (e.g. peach, apricot), cassava	chronic exposure may lead to thyroid and neurological disorders

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The chart below highlights the clinical picture for the various phases of IgG food sensitivity reactions. [Adapted from Dixon and Trevino. Food Allergy. 1997. Thieme Medical Publishing].

Clinical Phases of IgG Reactions		
I	Hidden Phase	Small amounts of the reactive food are eaten. Antibody-allergen complexes form, but are neutralized by the body. Patient is asymptomatic.
II	Symptomatic Phase	Reactive food is eaten in large quantities and regularly. Antibody-allergen complexes form and cannot be neutralized. Patient suffers chronic symptoms.
III	Trial Avoidance Phase	Patient removes reactive foods from diet. Levels of IgG antibodies to reactive foods remain high.
IV	Challenge Phase	Four or five days after reactive food antigens have been removed from diet, the food antigens have cleared but IgG antibody levels remain high. Patient consumes a large amount of the reactive food and experiences exacerbation of symptoms.
V	Elimination Phase	Reactive food is eliminated for 4 to 6 months. IgG levels to the reactive food(s) drop to non-reactive levels.
VI	Reintroduction Phase	After avoiding for 6 months, the reactive food is reintroduced. Patient to consume only modest amounts every fifth day. IgG levels rise when reactive food is consumed but because levels are already low, the elevation in IgG is usually insufficient to induce symptoms. Patient may consume modest amounts of the reactive food once every 5 days. Note that it is not always possible to reintroduce reactive foods into the diet without symptoms reappearing. In some cases, it may be necessary for the patient to permanently avoid the reactive food(s).

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