

Food Antibody *Assessment*

Overview Food allergy is defined as the immunologically mediated adverse reactions to foods.¹ Both food and environmental allergies have been implicated in a wide range of medical conditions affecting virtually every part of the body—from mildly uncomfortable symptoms such as indigestion and gastritis, to severe illnesses such as celiac disease, arthritis, and chronic infection. Allergies have also been directly linked to serious disorders of the central nervous system including: depression, anxiety, and chronic fatigue.^{2,3}

Food allergy causes the immune system to synthesize and release reactive chemical agents, such as histamines, cytokines, lymphokines, and interferons. These hormone-like substances can dramatically influence cellular physiology, producing far-reaching effects on the immune, endocrine, and nervous systems.

Genova Diagnostics' Food Antibody Assessment is unique. This profile targets not only likely causes of immediate (IgE) allergic reactions, but also possible sources of delayed (IgG) reactions—the so-called “hidden allergies,” whose effects may not show up for hours or even days after exposure to an antigenic substance. In addition, spices, inhalants and molds can be assessed to gain a greater insight into the etiological offending antigen(s).

Using state-of-the-art ELISA technology, the Genova Diagnostics automated Food Antibody Assessments measure relative levels of antibodies of the most commonly encountered types of foods. Armed with the information provided by these comprehensive assays, the physician can design a specific treatment program to reduce or eliminate exposure to antigenic substances that can trigger inflammatory reactions.

Food Antibody Assessments are also valuable as a preventive measure for patients who are not currently experiencing the overt symptoms of an allergic reaction. Elevated levels of antibodies can signify subclinical immune reactions which, if ignored, may place cumulative stress on the immune system over time—setting the stage for the development of illness in the future.

History of Food Allergy

The recognition of food sensitivity was first recorded by Hippocrates, who observed that milk could cause gastric upset and urticaria. In 200 A.D. Galen described a case of allergy to goat's milk and in 1679 Willis observed that the ingestion of wine could precipitate asthma.

Soon after the turn of the century, Shloss described several cases that established a strong correlation between food allergy and the pathogenesis of atopic dermatitis.⁴ W.W. Duke was one of the first to make extensive observations of foods causing allergic responses. In the early 1920s, Duke published several papers linking food ingestion to bladder pain, Meniere's syndrome, colitis, gastro-intestinal (GI) upset, and diarrhea.^{5,6} Not long afterward, Walzer and his colleagues performed experiments clearly demonstrating how ingested food antigens penetrate the GI barrier and are transported through the bloodstream to mast cells in the skin.^{7,8}

In the 1930s, Rinkel first described food sensitivities that differed from the classic immediate anaphylactic reactions. The symptoms he described occurred hours or days subsequent to ingestion and could be masked or unmasked by the offending food.⁹ Rinkel's discovery has been borne out by recent research confirming that delayed-type food allergies play a primary role in the immune system's response to ingestants.¹⁰

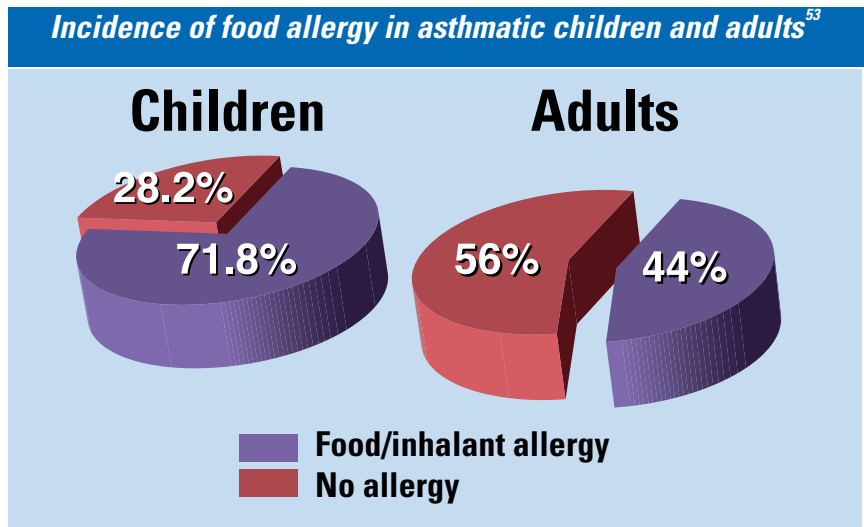
What this test does:

Identifies antibodies related to immediate (IgE) and delayed (IgG) hypersensitivities to foods.

Provides qualitative and quantitative information related to both immediate and delayed-onset hypersensitivity reactions.

Includes an individualized True Relief™ rotation diet schedule categorized into food families and related foods

Turn-around Time: 7 calendar days



Allergies Today

Significant progress has been made towards our understanding of food allergies, particularly in the last five years. A number of food allergies have now been characterized at the molecular level. This has given the clinician valuable insight into the immunopathogenesis of many allergic disorders.¹¹

It is now estimated that up to 20% of the population have adverse reactions to foods and nearly 4% of Americans have immune mediated allergies. Atopic dermatitis now affects 10-20% of children and 1-3% adults worldwide and the prevalence increases as countries become more industrialized.^{12,13}

Some physicians even claim that food allergies are a leading cause of most undiagnosed symptoms. As one investigator noted, "The management of allergic diseases involves considerable financial and other costs. In industrialized countries, atopic disease is the commonest cause of morbidity and a significant factor in mortality."¹⁴

Why has the incidence of allergy risen so dramatically? Food products most frequently incriminated in allergic reactions are often hidden as ingredients in commercial foods.¹⁵ Many modern foods, as well as medicinal drugs such as penicillin, also contain preservatives, stabilizers, artificial colorings, and flavorings. Some scientists believe that increased chemical pollution in our air, water, and food is to blame. Foods can easily become contaminated by the use of insecticides in farming.

The multifactorial causes currently under investigation include: genetic atopic predisposition, allergen exposure and sensitization in early childhood, viral respiratory tract infections in young children, smoking during pregnancy, poor quality diet, reduced breast-feeding, childhood obesity, immunologic predisposition (Th2-prone), environmental pollution, and childhood immunization.¹⁶

Other possible reasons for increased food hypersensitivity include genetic manipulation of plants, resulting in food components which cross-react with normal tissues; less diversity in the diet, cultural differences and route of exposure. The way in which we process and cook foods along with our individual digestive capacity can also increase food hypersensitivities.¹⁷

Cause and Development

It is well-documented that food allergy is an expression of an inherited genetic predisposition.¹⁸ Hence, allergic histories can often be found in both parents and siblings. One study discovered that when both parents are allergic, 67% of the children are also allergic. When only one parent is allergic, 33% are allergic.¹⁹

Inadequate digestion of food products due to hypochlorhydria and/or pancreatic enzyme deficiency is also thought to be a significant cause of food allergies. Insufficient brush border enzymes such as lactase and sucrase also affect the body's ability to breakdown food to an elemental form.²⁰

When proteins are not digested to amino acids, dipeptides, or short chain polypeptides, they retain their antigenic properties. These antigenic molecules may then be absorbed

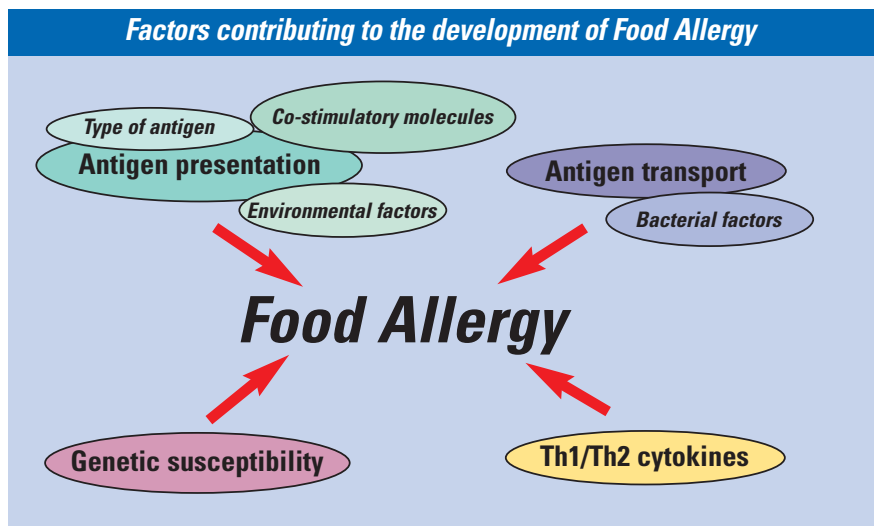
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through a damaged mucosal barrier or “leaky gut” and exposed to the immune system. This in turn can create a state of chronic immune hypersensitivity and inflammation. In general, foods with a higher protein content (>20%) are more likely to be allergenic.²¹

Allergy Symptoms

Food and environmental allergies have been linked to a wide range of medical conditions affecting virtually every part of the body. They have been shown to cause migraines,²² depression,²³ eczema,²⁴ sinusitis,²⁵ arthritis,²⁶ colitis,²⁷ ear infections,²⁸ childhood hyperactivity,²⁹ urticaria,^{30,31} asthma,³² and many other pathological conditions. Any of the symptoms shown in Table 1 (next page) should make the clinician suspect possible food allergies. Gastrointestinal dysfunctions such as peptic ulcer, dyspepsia, gastroduodenitis, and hiatal hernia may promote some of these adverse reactions to food.³³

What is interesting is that 90% of the recognized food allergies are essentially caused by eight foods or food groups. The most common allergens include: eggs, dairy, wheat, soy, peanut, tree nuts, fish and shrimp.^{34,35}



The Role of the Immune System

The immune system is a complex molecular network with specific functions that defend the human host against invading organisms. There are two types of immunity the body develops to protect itself: innate immunity and acquired immunity.

Innate Immunity

When functioning properly, the immune system has the ability to resist organisms and toxins that damage human tissue. Resistance includes:

- 1) Phagocytosis of bacteria and other invaders by white blood cells and cells of the macrophage system.
- 2) Destruction of organisms by the hydrochloric acid secretion of the stomach.
- 3) Integumentary defense.
- 4) Destruction of foreign organisms or toxins by chemical compounds in the bloodstream (eg lysozyme, complement complex, polypeptides, natural killer cells).

Acquired Immunity

Acquired immunity is the human body's ability to develop extremely powerful specific immunity against individual invading antigens such as lethal bacteria, viruses, toxins, etc. There are two basic types of acquired immunity:

- 1) Humoral, or B-cell, immunity, which involves the production of circulating antibodies.
- 2) Cell-mediated, or T-cell, immunity, which involves the formation of large numbers of activated lymphocytes specifically designed to destroy the foreign agent.

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Acquired Immunity and T Helper Lymphocytes

The immune system is constantly working to achieve a balance between immunity and tolerance, in other words, between inflammation and unresponsiveness.³⁶ Whether the immune response is going to be a cell mediated or humoral response is determined by the balance between two subpopulations of T helper cells; Th1 and Th2.

There are several factors that affect the differentiation of a T cell into a Th1 or Th2 lymphocyte; age, genetic background, target organ involved, type of antigen, transforming growth factor and cytokine modulation.³⁷

In the presence of the cytokines interferon-gamma (IFN-g) and interleukin-2 (IL-2) an undifferentiated T cell will transform into a Th1 lymphocyte, whereas IL-4 and IL-5 stimulation produces a Th2 cell.

Th2 cytokines promote IgE production and mast cell growth and differentiation.

The cytokine IL-4 results in undifferentiated T cells transforming into Th2 lymphocytes which further stimulates IgE production. IL-5 affects eosinophils, causing them to ultimately degranulate within the tissues with subsequent respiratory epithelial damage.³⁸

Allergic individuals have been found to have a Th2 (IL-4, IL-5) cytokine pattern, whereas non-allergic subjects have a Th1 (IFN-g, IL-2) cytokine pattern.³⁹ It therefore appears that Th1/Th2 imbalance can determine if the food allergy response is going to be IgE mediated, non-IgE mediated, or a combination of the two.⁴⁰

Th1/Th2 Balance and the Hygiene Hypothesis

During pregnancy and in early infancy, there is a shift in the Th1/Th2 balance towards Th2 dominance. The gestational shift is thought to be a healthy phenomena that is advantageous for the survival of the fetus. In healthy infants, Th1 increases during the first year of life with a resultant balance between the differentiated T lymphocytes. In the atopic individual however, there is a skewing towards Th2 dominance.⁴¹

Research has demonstrated a 2-3 fold increase in the prevalence of asthma and atopia in children from industrialization countries. This Westernized effect is thought to be an example of the hygiene hypothesis. While several factors are thought to contribute to this hypothesis, ongoing research is conflicting. Some of the proposed factors have included; an inverse relationship to birth order and atopia, rising socio-economic status, vaccinations, and reduced exposure to microbial pathogens in early life. The consistent findings in the literature appear, in part, to relate to "the immunomodulatory effects of different patterns of neonatal gut colonization".⁴³

Common Symptoms of Food Allergies

Gastrointestinal <ul style="list-style-type: none">• vomiting• diarrhea• gas• infantile colic• abdominal pain and colic• loss of appetite• constipation• malabsorption• gastritis• ulcerative colitis• intestinal hemorrhage• functional intestinal obstruction• duodenal ulcer• irritable bowel syndrome• celiac disease• weight gain	Auto-Immune <ul style="list-style-type: none">• rheumatoid arthritis• Systemic Lupus Erythematosus(SLE)• Ankylosing Spondylitis(ALS)• multiple sclerosis	Respiratory <ul style="list-style-type: none">• coughing and wheezing• chronic rhinitis• asthma• recurrent bronchitis• recurrent croup• recurrent otitis media• hemoptysis	Genitourinary <ul style="list-style-type: none">• bed-wetting• chronic bladder infections• nephrosis
Musculoskeletal <ul style="list-style-type: none">• joint pain• low back pain• bursitis	Neurological <ul style="list-style-type: none">• headache• fatigue• insomnia• irritability• hyperkinesia• depression• anxiety• personality change• seizures• migraines	Immune <ul style="list-style-type: none">• chronic or recurrent infections	Others <ul style="list-style-type: none">• fainting• hypoglycemia• anemia• sinusitis• eosinophilia• arrhythmia• failure to thrive
	Dermatologic <ul style="list-style-type: none">• acne• canker sores• eczema• itching• rash• urticaria (hives)• angioedema• dermatitis		

Table 1

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In industrialized countries, hygienic measures begin as early as the birthing process, which disrupts the neonates capacity to uptake the mother's gut microflora. As a consequence, different microflora are established in the infant. Instead of harboring *Escherichia coli*, newborns are more often colonized with *Staphylococcus aureus*, which can originate from the mother's nose and/or breasts. The lipopolysaccharide content from beneficial *E. coli* is thought to help develop tolerance, that is to help stimulate Th1 or cell mediated immunity. *Staphylococcus aureus* favors a Th2 immune response and has been found to induce the synthesis of IgE antibodies in nearly 60% of atopic patients.⁴⁴ This shift in microbial flora is thought to set the stage for Th2 predominance and increased potential for allergies.⁴⁵

Food Allergies and Irritable Bowel Syndrome (IBS)

While clinicians don't always recognize food hypersensitivity as a cause for IBS, 20-65% of patients have related their symptoms to negative food reactions.⁴⁶

Nanda et al studied the effects of an exclusion diet in 200 IBS patients and reported a 48% improvement in symptoms.⁴⁷

The pathogenesis of food hypersensitivity induced IBS is thought to relate to the effects of IgE and IgG mediated mast cell degranulation. The release of histamine and other inflammatory mediators results in abnormal bowel motility, altered secretory response and increased mucosal sensitivity, which are symptoms characteristic of IBS.

A recent article in *Gut* demonstrated the effectiveness of IgG testing in IBS. In this cohort of patients, elimination diets were incorporated based upon IgG reactivity with a significant reduction in symptoms.⁴⁸ Interestingly, food allergy as an underlying etiology in IBS appears to be more common in those with diarrhea predominant IBS.⁴⁹

As IBS is considered a multifactorial condition, testing patients with the Allergy Antibody Assessment will quickly determine if IgE and/or IgG mediated food allergies are involved.

Relationship between Allergies and the Immune System

Acquired immunity is extensively involved in allergic reactions. Substances that initiate immune responses are known as antigens. Generally, antigens are proteins or large polysaccharides having a high molecular weight (8000 Da or greater).

Food represents the largest antigenic challenge confronting the human immune system.⁵⁰ As Sid Baker, M.D., has pointed out, the surface area of the GI tract is greater than the area of a tennis court, making it the largest, most active immune-reacting surface in the body. Immunologically mediated food hypersensitivity is the result of interactions among ingested food antigens, the digestive tract, tissue mast cells, circulating basophils, and food-antigen-specific immunoglobulins.

There are five major classes of immunoglobulins—IgA, IgD, IgE, IgG, and IgM. ("Ig" stands for immunoglobulin and the other letter simply designates the class of the antibody.) IgE defends against parasitic infection and is known as the reaginic antibody for its major role in instigating immediate allergic responses to foods and other environmental antigens. The other immunoglobulins appear to be more involved in less immediate reactions. Of these, IgG is the most abundant, comprising about 80% of all circulating antibodies.⁵¹

Types of Immune Reactions

Although the function of the immune system is to protect the host from foreign antigens, abnormal or prolonged immune responses can lead to tissue injury and disease.

Food allergy reactions are just one expression of this type of immune-mediated damage. Gell and Coombs have classified the mechanisms of immune tissue injury into four distinct types:⁵²

Type I: Immediate hypersensitivity reactions

These reactions occur less than 2 hours after contact with allergens. Antigens bind to pre-formed IgE antibodies already attached to the surface of the mast cell or the basophil and cause the release of chemical mediators such as histamine and eosinophilic chemotactic factor. A variety of allergic symptoms may result, depending on the location of the mast cell: in the nasal passages there may be sinus congestion; in the bronchioles,

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constriction (asthma); in the skin, hives and eczema; in the synovial cells, arthritis; in the intestinal mucosa, inflammation with resulting intestinal spasm or malabsorption; and in the brain, headaches, loss of memory, and inability to concentrate.

Type II: Cytotoxic reactions

These reactions involve the binding of either IgG or IgM antibodies to cell-bound antigen. The antigen-antibody binding activates the complement cascade, resulting in damage to the cell to which the antigen is bound. Erythrocytes and platelets are the cells most commonly affected with cytotoxic hypersensitivity.

Type III: Immune complex-mediated reactions

Immune complexes are formed when antigens bind to antibodies. If not excessive, and assuming a healthy immune response, these complexes are usually cleared from the circulation by the phagocytic system. However, deposition of these complexes in tissues or in vascular endothelium can produce immune complex-mediated tissue injury. This tissue damage is further enhanced by the presence of vasoactive amines, which increase vascular permeability and promote the deposition of more immune complexes.

Type III responses are usually delayed, occurring hours or even days after exposure. They have been shown to involve both IgG and IgE immune complexes.^{53,54}

Type IV: T-cell dependent reactions

This delayed-type reaction is mediated primarily by T-lymphocytes, after an allergen makes contact with a mucosal surface. By stimulating sensitized T-cells, inflammation may result within 36 to 72 hours after contact. A Type IV reaction does not involve antibodies.

Role of IgE and IgG

IgE antibodies are believed to trigger allergic reactions when they crosslink on the surface of gastrointestinal mast cells, stimulating the release and production of chemical mediators such as histamine, proteoglycans, and leukotrienes. These potent reactors instigate a barrage of effects on surrounding intestinal tissue and, by inducing intestinal permeability, may also allow passage of food antigens into the bloodstream. When this happens, other organs in the body then become targets for the allergic reaction; further involvement with other cell types in the body may result in the creation of a chronic, perpetual immune response.

Since most severe, immediate allergy symptoms are IgE-mediated, many doctors have limited their testing to this class of immunoglobulins. Certainly, an abundance of medical literature supports using the IgE assay as a means of diagnosing Type I allergic reactions.^{55,56,57,58,59} There is also considerable evidence, however, underscoring the significance of IgG as a marker in allergy testing as well.

Repeated exposure to an antigen can eventually produce allergy-like responses, or hypersensitivities. These reactions are usually delayed, with symptoms that may not surface until hours, or even days, after the initial exposure. Although IgE may be involved, it is theorized that these delayed reactions are primarily mediated by IgG.

One study assessed IgG levels in 114 patients with a history of delayed food allergies. An elimination diet was then implemented as a sole means of treatment with a 71% overall success rate. What was most impressive was the improvement in the group of patients with chronic symptoms previously unresponsive to therapy. 20% of this cohort experienced a 100% relief of symptoms simply from dietary avoidance of IgG reactive foods.⁶⁰

Specific IgE has a half-life in circulation of one to two days, and a half-life on the mast cell of about 14 days. IgG, on the other hand, appears to have a circulating half-life of 21 days, with a residual time on the mast cells that can last as long as 2-3 months.⁶¹ Thus an IgG assay is an essential tool for diagnosing the possible causes of delayed, non-anaphylactic responses, the so-called "hidden" allergies, which cannot be detected with conventional IgE tests such as radioallergosorbent test (RAST) or skin testing.

Numerous studies indicate a role for IgG in non-IgE, mast-cell mediated diseases as well as various food allergies.^{62,63,64,65} IgG can induce basophil degranulation, triggering the release of histamine and other potent chemical mediators upon exposure to specific antigens—a common mechanism of allergic reactions.⁶⁶

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In one study, individuals with hypersensitivity to shrimp were determined by double-blind, placebo controlled challenges. Shrimp-specific IgE and IgG, but not IgM and IgA, were significantly higher in the group with shrimp hypersensitivity as compared to controls.⁶⁷ Another group of researchers verified that children with atopic eczema showed much higher levels of IgG antibodies to casein and ovalbumin subclasses than did controls.⁶⁸

IgG and Physiological Function

Besides providing a means for diagnosing suspected antigens, IgE and IgG can have crucial implications for gastrointestinal and immune function. Since IgG antibodies have been detected in a wide range of circumstances in health and in disease, there are researchers that have questioned their clinical significance. Some scientists believe IgG antibodies to be a "normal response to protein that crosses the intestinal mucosal membrane" while others have demonstrated a clear correlation to food allergy.⁶⁹ One consistent and important finding in patients with high circulating IgG levels, is the alteration in mucosal membrane integrity.⁷⁰

Thus, high levels of IgG to food antigens have been found in other disease conditions associated with increased intestinal permeability, such as IgA deficiency, Celiac and inflammatory bowel disease (IBD).^{71,72} This increased permeability is believed to be caused by a selective transport mediated by receptors on epithelial surfaces. By increasing intestinal permeability, elevated levels of IgG could result in increased exposure to antigens. Since increased intestinal permeability has been implicated in a number of disorders, elevated levels of IgG may also shed light on the cause of concomitant local and systemic disease states.

Oral Challenge, RAST and Skin Testing

The double-blind, placebo-controlled food challenge (DBPCFC) is considered the gold standard in diagnosing food allergies.⁷³ This procedure can be somewhat invasive (requiring subjects to have food antigens administered via a nasogastric tube), is time consuming and potentially dangerous if the reaction is severe.⁷⁴ In addition, the DBPCFC is only able to confirm specific food reactions based upon patient history and prior evaluation.⁷⁵

Conventional skin testing and RAST tests measuring IgE-mediated reactions cannot guide physicians as to the potential for delayed, non-IgE-mediated reactions.⁷⁶ In one study, researchers surmised that because an IgG subclass was involved in late-onset reactions, patients exhibiting delayed bronchial allergic reactions failed to show positive skin test reactions or RAST results to a specific allergen.⁷⁷ A recent study by Jahn-Schmid et al, demonstrated the increased sensitivity of ELISA testing in detecting food allergies when compared with RAST testing.⁷⁸

Skin testing, while a valuable indicator of IgE mediated reactions also has its limitations. This diagnostic test should ideally be performed by a skilled physician as it may trigger life-threatening symptoms such as anaphylaxis.⁷⁹

The Food Antibody Assessment

The **Food Antibody Assessment** identifies IgG antibodies to a vast array of food substances using panels for 88 foods. There is also a panel for IgE antibodies to 19 of the most common allergenic foods as well as a total IgE measurement. Additional profiles are available for a more comprehensive antigen assessment. These include an **IgG Vegetable Add-On Profile**, an **IgG Spices Profile**, an **IgG Inhalants Profile** and an **IgE Molds Profile**. Each additional profile may be ordered separately or combined.

IgG Vegetable Add-on Profile

The **IgG Vegetable Add-on Profile** is a beneficial extension of the Food Antibody Assessment for vegetarians or those with a varied diet. This Add-on profile evaluates IgG for 21 vegetarian foods, including grains, fruits, nuts, and beans. This panel includes artichoke, bean sprout, cantaloupe, cashew, cherry, coconut, flax seed, garbanzo, filbert, kamut, millet, mung bean, navy bean, oat bran, parmesan cheese, pistachio, safflower, triticale, watermelon, wheat bran, and wild rice.

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IgE Inhalants, IgE Molds, and IgG Spices Profiles

Hypersensitivities to foods can also occur as a consequence of sensitization to inhalant allergens. A syndrome known as the pollen-food allergy or oral allergy syndrome can occur when inhaled pollens that patients are sensitized to (such as birch, ragweed and mugwort) cross react with plant proteins. These patients often experience symptoms in the oral and pharyngeal mucosa.⁹⁰

The **IgE Inhalants Profile** measures relative levels of antibodies to 18 region-specific inhalants. It is customized to include common allergens found in any one of 18 geographic regions throughout the United States, and Canada.

The **IgE Inhalants Profile** includes a total reactivity result for general molds. Should this general test be positive, the clinician may want to determine the specific mold(s) affecting a patient. The **IgE Molds Profile** should then be performed.

An elevated total IgE on the **Food Antibody Assessment** with negative individual IgE food results should direct the clinician towards additional IgE Inhalants and Mold testing.

The **IgG Spices Profile** determines separate IgG titers for 24 commonly used spices.

Antibody Testing with ELISA

A detailed and comprehensive analysis is crucial for the clinician to make accurate, precise diagnoses of food and environmental allergies. With the Allergy Antibody Assessment, IgE and IgG levels are assessed using an Enzyme-Linked Immunosorbent Assay (ELISA). This advanced immunological procedure uses an enzyme binding process to detect antibody levels, and has been hailed as a “safe, economical, and highly sensitive test.”⁹¹

Because the ELISA method identifies antibodies associated with both immediate and late-onset, delayed reactions, it offers a clear advantage over other conventional food antibody assessments.

Genova Diagnostics now has a new, highly specialized methodology for IgE testing. The enzyme linked immunosorbent assay (ELISA) technology is standardized against the World Health Organization (WHO) International Reference Preparation to ensure assay validation and the highest quality control. Cross reactivity is practically non-existent (<0.0001%) against other immunoglobulins, namely IgA, IgG and IgM. Total IgE levels are reflective of overall circulating IgE, whereas antigen-specific IgE measurements reflect the level of IgE pertaining to the antigen tested. With this new methodology, quantitative (rather than semi-quantitative) results can be determined for all the IgE foods tested. This means that results are expressed in concentration units as well as class scores. When measured in this way, the clinician can easily and more effectively monitor changes in clinical allergenicity over time.

Our User-Friendly Report

The Food Antibody Assessment features a “stop-light” system of color-coding that shows at a glance which foods should be avoided or rotated. Foods associated with a “high” relative antibody level are in the red zone and should be eliminated from the diet for a period of time. Foods associated with non-detectable antibody are indicated by “0”. Those associated with a very low amount of antibody are indicated in green, while low and intermediate levels of antibodies are indicated in yellow and pink respectively. This unique report presentation allows both patients and physicians to quickly grasp test results.

By providing separate ratings for both IgE and IgG antibodies, the report form enables the clinician to evaluate the influence of IgE and IgG independent of each other, while still allowing both panels to be viewed together for a composite analysis. A total IgE on the report shows the overall degree of IgE reactivity, and when positive, alerts the clinician to additional inhalant testing. Since IgE and IgG each have different clinical presentations, the clinician will find the separate panels on the one report extremely useful.

Clinical Therapeutics

True Relief™, a medically advanced rotation diet and one of the many innovative features of the IgG Food Antibody Assessment, is a personalized treatment plan based on individual

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test results. The **True Relief™** guide will accompany each IgG Food Antibody Assessment report, with a general discussion of food allergy, food families, related foods, elimination of allergenic foods, rotation diet, and reintroduction of foods. The rotation diet will let patients see at a glance their problem foods and dietary choices.

The **True Relief™** guide offers greater flexibility to clinicians in their approach to their patients. Because it is highly adaptable, the implementation of the **True Relief™** rotation diet is determined by the patient and clinician together.

In this way, **True Relief™** can be a powerful tool for developing a successful allergy treatment program—simplifying treatment protocol, saving valuable time, and encouraging patient compliance.

Working with Results

The reported relative level of antibodies to various foods indicates an immune response to those foods. Such sensitivities may or may not correlate with clinical symptoms, but should be regarded as antigen-triggered immune responses which, if allowed to accumulate along with other stressors to the immune system, have the potential to lead to illness.

In general, oligoantigenic (low allergy) diets have proven highly effective in treating a diverse range of allergic responses. Children with Attention Deficit Disorder (ADD) showed a marked improvement in their hyperactive behavior following the removal of provoking foods from their diets.⁸² In another study, 93% of 88 children with severe frequent migraine recovered on an oligoantigenic diet—even in instances when the migraines were provoked by additional factors such as blows to the head, exercise, or flashing lights.⁸³ A low allergen diet also significantly reduced symptoms of colic in infants and chronic urticaria with arthralgia in adult patients.^{84,85} Diversified rotation diets are often used to prevent new allergies from developing and to give the immune system a rest.⁸⁶

Food Allergy vs Food Intolerance

Periodically, results of the Food Antibody Assessment will reveal no allergies. This can be perplexing for both practitioner and patient, especially when there are obvious symptoms after food ingestion. What is important to understand, is that not all food reactions are immune mediated. In some patients, food intolerances, rather than food allergies can be the cause of their symptoms. A food intolerance defined, is an adverse physiologic response to a food, or given foods. Unlike true food allergies, food intolerances do not elicit an immunoglobulin response. They can result from factors inherent in a food such as salicylates, lectins, toxic contaminants, or can be due to the pharmacologic properties of the food (eg tyramine in aged cheeses). A food intolerance can also be due to metabolic disorders in the host. An example of this would be a lactose deficiency.⁸⁷

The physiological responses of food allergies and intolerances can mimic one another, making it challenging at best to differentiate the two. The Food Allergy Assessment Profile helps determine if adverse food reactions are true food allergies, or food intolerances. In this capacity, negative results, can be just as significant as tests revealing positive IgG and/or IgE responses. Refer to the article "*Toward An Understanding of Allergy and In-Vitro testing*" located on the Genova Diagnostics website, www.GDX.net, for more in-depth reading.

Therapeutic Considerations

Dietary exclusion of offending foods is an important component in the treatment of immune mediated allergies.⁸⁸ Essentially, for as long as the host is exposed to the reactive foods, an immunoglobulin response will persist. IgE allergies are considered permanent allergies, and avoidance needs to be life long. In contrast, IgG mediated allergies can be reversed over time after initial avoidance of reactive foods, and ongoing dietary rotation. In more serious cases, or in instances where allergens cannot be avoided, techniques such as Immunotherapy (hyposensitization) or Enzyme-potentiated desensitization (EPD) can be utilized to reduce symptoms. Medications that serve to palliate adverse reactions include; anti-histamines, decongestants and glucocorticosteroids. Another therapeutic approach is to prevent mast cells from degranulating and

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releasing histamine. Sodium cromoglycate⁹⁹ and the bioflavonoid quercetin⁹⁰ are both effective agents in blocking mast cell degranulation.

Current research suggests a promising role for the use of probiotics in the prevention and treatment of food allergies.⁹¹ Two recent studies have demonstrated a 50% reduction in atopia in infants when *Lactobacillus* GG was given during pregnancy and breastfeeding.^{92,93} Both *Lactobacilli* and *Bifidobacteria* have demonstrated anti-allergenic potential, though appear to have different clinical implications. *Lactobacilli* are effective in preventing atopia, whereas *Bifidobacteria* are capable of reversing the development of atopy.⁹⁴

While the exact mechanisms are not fully understood, their beneficial effects are thought to relate to restoring healthy flora, increasing secretory IgA (SIgA) and reducing gut permeability. Another way in which probiotics help prevent food allergies may relate to their effects on the Th1/Th2 balance. Beneficial microflora appear to encourage the differentiation of T lymphocytes into Th1 and Th3 thereby reducing the tendency towards Th2 IgE mediated allergic reactions.⁹⁵ Research on specific probiotic strains is underway and should help elucidate the exact mechanisms by which microflora exert their immunoregulatory effects.

Related Tests to Consider Intestinal Permeability Assessment

A healthy intestinal tract provides an effective barrier against excessive absorption of intraluminal dietary and microbial antigens.

With increased gut permeability, greater quantities of antigens are allowed to penetrate the GI barrier, resulting in an overly sensitized, reactive immune system in some individuals. Increased permeability has been implicated in Type I, Type II, and Type IV allergies.⁹⁶ F. Andre, a leading French researcher in the field of food allergy, found that contact between an allergen and the digestive tract significantly increased intestinal absorption of macromolecules.⁹⁷ In another study, C. Andre concluded that "evaluation of intestinal permeability... provides an objective means of diagnosing food allergy and assessing the effectiveness of anti-allergic agents."⁹⁸ Genova Diagnostics' Intestinal Permeability test evaluates the small intestine's effectiveness to act as a barrier to harmful macromolecules. The profile is also able to monitor changes in mucosal permeability, and help determine underlying causes of systemic problems linked to GI function.

Comprehensive Digestive Stool Analysis (CDSA)

Maldigestion of food products is considered a significant cause of food allergy.

When proteins are not digested properly to amino acids, dipeptides, or short chain polypeptides, they retain their antigenic properties. This in turn can trigger repeated responses by the immune system, possibly leading to a state of chronic hypersensitivity. The Comprehensive Digestive Stool Analysis can provide clues about the possible cause of food allergies by closely examining the digestion and absorption status of the gastrointestinal tract.

Some researchers have suggested that food allergy is not an immunological disease but a disorder of bacterial fermentation in the colon.⁹⁹ According to this theory, food intolerance is caused by a combination of factors, including reduced gut enzyme concentrations, imbalanced bacterial flora, and increased intestinal permeability.¹⁰⁰

Comprehensive Digestive Stool Analysis 2.0 (CDSA 2.0)

In addition to assessing digestion and gut ecology, the CDSA 2.0 contains immune markers to evaluate inflammation and mucosal damage. Calprotectin reflects neutrophil infiltration into the gut lumen, and has been found to be elevated with cow's milk enteropathy as well as multiple food allergies.¹⁰¹

Eosinophil Protein X (EPX) reflects the integrity of the gastro-intestinal mucosa. Proteins derived from eosinophils only enter the GI tract after damage to the connective tissue layer has occurred. Food allergies including Celiac disease have been associated with increased levels of EPX. Follow up testing enables practitioners to monitor dietary compliance as levels of both calprotectin and EPX reduce after elimination of food allergens.¹⁰²

Celiac Profile

Celiac disease is a genetic, immune mediated enteropathy of the small bowel that results in malabsorption. The disease is characterized by a sensitivity to the proteins found in wheat and to a lesser extent, barley, rye and oats.¹⁰³ Gastrointestinal manifestations can therefore mimic food allergies or irritable bowel syndrome. Individuals with a diarrhea-predominate IBS have a seven fold risk increased prevalence of celiac disease when compared with the general population.¹⁰⁴ Testing this patient cohort is therefore of value, and may help prevent years of morbidity, not to mention ongoing medical costs.¹⁰⁵

Helicobacter pylori Stool Antigen (HpSA) Test

There is increasing data that supports a significant association between *Helicobacter pylori* and food allergy.¹⁰⁶ *H. pylori* infection alters the integrity of the gastrointestinal mucosa which then allows intact molecules (such as food antigens) to cross the epithelial barrier. Corrado et al demonstrated a 56% positivity rate for *H. pylori* in children with atopia as a sole manifestation of food allergies.¹⁰⁷ This test can be ordered separately, or as an add on in the CDSA or CDSA 2.0.

ImmunoGenomic Profile

Cytokines have been shown to play a key role in the initiation and maintenance of allergy responses. This is because they are able to regulate IgE synthesis, and stimulate inflammatory cells such as mast cells and eosinophils. Single nucleotide polymorphisms (SNPS) in specific cytokines have been associated with allergic disease. Mutations in the cytokines IL-4 and IL-13 are associated with atopia, both of which are Th2 derived and strongly involved in IgE regulation.¹⁰⁸ The Th1 derived cytokine IL-10 can favor the tendency for food allergies in those who exhibit the polymorphism.¹⁰⁹

The ImmunoGenomic Profile can help clinicians tailor a treatment protocol based upon individual genetic susceptibility.

How do I order this test?

For Allergy Antibody Assessment kits or information, please call a Client Services representative at 800-522-4762 or order online at www.GDX.net.

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