Overview

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.

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. Because toxins can initiate a very similar set of reactions, food allergy and toxicity are considered intimately connected in a clinical sense. (See our Detoxification Application Guide.)

Great Smokies’ Comprehensive 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.

Using state-of-the-art ELISA technology, the automated Comprehensive Antibody Assessment measures relative levels of antibodies to over 120 of the most commonly encountered types of food and environmental substances. Armed with the information provided by this detailed and reliable assay, the physician can design a specific treatment program to reduce or eliminate exposure to antigenic substances that can trigger inflammatory reactions.

The Comprehensive Antibody Assessment is 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. 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, GI upset, and diarrhea. 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.

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. 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.

What this test does:
Identifies antibodies related to immediate and delayed hypersensitivities to over 120 food and environmental substances.

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

Turn-around Time 7 days
The incidence of food and environmental allergies and the number of atopic individuals have increased dramatically in recent times. Hypersensitivities involving bronchial symptoms and asthma, for example, have nearly doubled in the last decade.\(^8\) It is estimated that atopic dermatitis alone now affects between 10-15% of the population at some time during their lives, and that this condition is often directly provoked by food antigens.\(^9,10\)

Adverse reactions to food are now reported in about 25% of younger children.\(^11\) 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.”\(^8\)

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.\(^12\) 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.

Other possible reasons for increased food hypersensitivity include: earlier weaning and earlier introduction of solid foods to infants; genetic manipulation of plants, resulting in food components which cross-react with normal tissues; and less diversity in the average diet—leading to repeated exposure to food substances and the subsequent development of hypersensitivities. Probably all of these and more have contributed to the increased frequency and severity of allergic symptoms.

**Cause and Development**

It is well-documented that food allergy is an expression of an inherited genetic predisposition.\(^13\) 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.\(^14\)

Inadequate digestion of food products due to hypochlorhydria and/or pancreatic enzyme deficiency is also thought to be a significant cause of food allergies. 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 through a “leaky gut” and exposed to the immune system, creating a state of chronic immune hypersensitivity.
**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, eczema, thrombophlebitis, arthritis, colitis, enuresis, ear infections, gall bladder disease, childhood hyperactivity, hypotension, urticaria, asthma, glaucoma, and many other pathological conditions. Any of the symptoms shown in Table 1 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.

**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 acid secretion of the stomach.
3) Integumentary defense.
4) Destruction of foreign organisms or toxins by chemical compounds in the bloodstream (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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**Common Symptoms of Food Allergies**

<table>
<thead>
<tr>
<th>Gastrointestinal</th>
<th>Auto-Immune</th>
<th>Respiratory</th>
<th>Immune</th>
<th>Dermatologic</th>
<th>Genitourinary</th>
<th>Others</th>
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<tbody>
<tr>
<td>• vomiting</td>
<td>• rheumatoid arthritis</td>
<td>• coughing and wheezing</td>
<td>• chronic or recurrent infections</td>
<td>• acne</td>
<td>• bed-wetting</td>
<td>• fainting</td>
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<tr>
<td>• diarrhea</td>
<td>• Systemic Lupus</td>
<td>• chronic rhinitis</td>
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<td>• canker sores</td>
<td>• chronic bladder infections</td>
<td>• hypoglycemia</td>
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<td>• gas</td>
<td>• Erythematous(SLE)</td>
<td>• asthma</td>
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<td>• eczema</td>
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<td>• infantile colic</td>
<td>• Ankylosing Spondylitis(ALS)</td>
<td>• recurrent bronchitis</td>
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<td>• itching</td>
<td>• sinusitis</td>
<td>• sinusitis</td>
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<td>• abdominal pain and colic</td>
<td>• multiple sclerosis</td>
<td>• recurrent croup</td>
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<td>• rash</td>
<td>• eosinophilia</td>
<td>• eosinophilia</td>
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<tr>
<td>• loss of appetite</td>
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<td>• recurrent otitis media</td>
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<td>• urticaria (hives)</td>
<td>• arrhythmia</td>
<td>• arrhythmia</td>
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<td>• constipation</td>
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<td>• hemoptysis</td>
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<td>• failure to thrive</td>
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<td>• weight gain</td>
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</tbody>
</table>

Musculoskeletal

- joint pain
- low back pain
- bursitis

Neurological

- headache
- fatigue
- insomnia
- irritability
- hyperkinesis
- depression
- anxiety
- personality change
- seizures
- migraines

Respiratory

- coughing and wheezing
- chronic rhinitis
- asthma
- recurrent bronchitis
- recurrent croup
- recurrent otitis media
- hemoptysis

Immune

- chronic or recurrent infections

Dermatologic

- acne
- canker sores
- eczema
- itching
- rash
- urticaria (hives)
- angiodema
- dermatitis

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Acquired immunity is extensively involved in allergic reactions. Substances that initiate immune response 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.27 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.28

Although the function of the immune system is to protect the host from foreign antigens, abnormal 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:27

**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, 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.

**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 IgM immune complexes.29,30

**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. There is also considerable evidence, however, underscoring the significance of IgG as a marker in allergy testing as well. In fact, it is estimated that IgG and IgG complex mediators are involved in 80% of all food allergy reactions.

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. One study found that nearly 60% of patients with food intolerance exhibited late (delayed), rather than early or immediate reactions to provoking foods.

Although IgE may be involved, it is theorized that these delayed reactions are primarily mediated by IgG. 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. 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. 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.

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. 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.

**IgE/IgG and Physiological Function**

Besides providing a means for diagnosing suspected antigens, IgE and IgG can have crucial implications for gastrointestinal and immune function. In experimental models, IgG antibodies have been shown to increase intestinal permeability.

Thus, high levels of IgG to food antigens have been found in other disease conditions associated with increased intestinal permeability, such as IgA deficiency and inflammatory bowel disease. This increased permeability is believed to be caused by a selective transport mediated by Fc receptors on epithelial surfaces. By increasing intestinal permeability, undetected elevated levels of IgG could result in increased exposure to antigens.

Production of IgG and IgE is controlled by at least two cytokines, interleukin-4 (IL-4) and interferon-gamma (IFN-g). Since there is evidence that increased synthesis of IgG and IgE is a result of decreased inhibitory effect of IFN-g, it is postulated that defective immunoregulation involving IL-4 and IFN-g both sustains and increases the synthesis of IgG and IgE antibodies.
Comprehensive Antibody Assessment

RAST, Skin, and Oral Challenge Testing

Although many food allergy experts regard oral challenge testing for immediate food hypersensitivities as accurate and reliable, it is time-consuming and potentially dangerous if the reaction is severe. Conventional skin testing and RAST tests measuring IgE-mediated reactions cannot guide physicians as to the potential for delayed, non-IgE-mediated reactions. 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. In addition, there are clinical situations where skin-testing is unfeasible and may inadvertently trigger life-threatening symptoms.

The Comprehensive Antibody Assessment

The Comprehensive Antibody Assessment identifies both IgE and IgG antibodies to a vast array of food substances using panels for 88 combined foods or 88 vegetarian foods. In addition to the food antibody panel, the comprehensive assessment includes an IgE Inhalants Profile measuring relative levels of antibodies to 36 region-specific inhalants. The Inhalants Profile is customized to include common allergens found in any one of five regions of the continental United States: Northeast, Southeast, Southwest, West, or Northwest. If a region is not specified on the Comprehensive Antibody Assessment or Inhalants Profile Requisition Form, a region will be selected on the basis of the ordering physician’s return address. (A list of allergens appearing in most of the individual profiles is shown in Table 2. A list of individual components for each specific region is available upon request.) Each panel may be ordered separately.

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 Comprehensive 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.” 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.

Our User-Friendly Report

The Comprehensive 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 no 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. 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. Since IgE and IgG each have different clinical presentations, the clinician will find the separate panels extremely useful.

Clinical Therapeutics True Relief™: a Medically Advanced Rotation Diet

One of the many innovative features of the Comprehensive Antibody Assessment is a personalized treatment plan based on individual test results. True Relief™, a customized advanced rotation diet guide, will accompany each food antibody assessment form, with a general discussion of food allergy, food families, related foods, elimination of allergenic foods, rotation diet, and reintroduction of foods. The rotation
Comprehensive Antibody Assessment

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 diets have proven highly effective in treating a diverse range of allergic responses. Children with Attention Deficit Disorder showed a marked improvement in their hyperactive behavior following the removal of provoking foods from their diets. 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. A low allergen diet also significantly reduced symptoms of colic in infants and chronic urticaria with arthralgia in adult patients. Diversified rotation diets are often used to prevent new allergies from developing and to give the immune system a rest. For specific treatments, please refer to our report supplement.

Related Tests to Consider

Intestinal Permeability

A healthy intestinal tract provides an effective barrier against excessive absorption of food 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. 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. 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.” Great Smokies’ Intestinal Permeability test evaluates the small intestine’s effectiveness as a barrier to macromolecules, monitors changes in mucosal permeability, and determines 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. 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 (also known as “leaky gut syndrome”). See GSDL’s Comprehensive Digestive Stool Analysis Application Guide for more information on this.

24 Spice Profile

A natural extension of the Comprehensive Antibody Assessment, this assay determines separate IgE and IgG titers for the 24 commonly used spices shown in Table 3.
Comprehensive Antibody Assessment

Vegetarian Add-On Panel
This extension of the Food Antibody Assessment evaluates IgE and 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.

Anti-Chemical Antibodies Profile
The preponderance of synthetic chemicals used in manufacturing today, combined with the increased time spent in indoor environments, pose a health threat to many individuals with sensitized immune systems. The Anti-Chemical Antibodies Profile measures systemic exposure and antibody levels to formaldehyde (FMA), trimellitic anhydride (TMA), toluene di-isocyanate (TDI), phthalic anhydride, and benzene ring. Exposure sources include carpet, glues, cosmetics, plastics, paints, epoxy resins, and car exhaust. The profile provides separate panels for IgE, IgG, and IgM antibodies.

Adrenocortex Stress & Melatonin Profiles
Since the etiology of food and environmental allergy involves interaction among numerous chemical mediators in the immune system, including cortisol, many sensitized individuals commonly exhibit various endocrine dysfunctions. Moreover, the severity of allergy symptoms often follows a chronobiologic pattern, highly influenced by circadian hormone rhythms. Great Smokies’ Adrenocortex Stress Profile and Comprehensive Melatonin Profile can help you assess how adrenocortical and pineal gland function may be adversely affecting hypersensitivity conditions.

Anti-Gliadin Antibodies (Salivary)
Gliadin is the fraction of gluten which is most toxic to individuals who are sensitive to gluten. As the predominant immuno-globulin of intestinal secretions, secretory IgA reveals the specific mucosal response to toxic antigens such as gliadin. Elevated anti-gliadin IgA antibodies in the saliva are a definitive clinical marker of gliadin intolerance with mucosal involvement.

How do I order this test? For Comprehensive Antibody Assessment kits or information, please call a GSDL Accounts Receivable representative at 888-201-8333 or use our secure web contact center at www.gsdl.com/billing.