

ARRAY 4

ARRAY 4 – Antibody

**GLUTEN-ASSOCIATED SENSITIVITY
& CROSS-REACTIVE FOODS™**



TABLE OF CONTENTS

[Overview](#)

[Clinical](#)

[Specimen Requirement](#)

[Related Testing](#)

[References](#)

GLUTEN-ASSOCIATED SENSITIVITY AND CROSS-REACTIVE FOODS™

OVERVIEW

Once a patient is properly diagnosed as Gluten-Sensitive or having Celiac disease, he/she is instructed to adhere to a gluten-free diet. Brochures, books and websites help the patient with this seemingly difficult process. However, a significant percentage of these patients will continue to have gluten-like complaints even after being on a gluten-free diet for months. Most countries define “gluten-free” products based on the recommendation of the Food and Agricultural Organization of the United Nations and World Health Organization. This codex alimentarius allows the inclusion of up to 0.3% protein from gluten containing grains in foods labeled “gluten-free.” If the sensitive body is exposed to 0.3% protein, the immune system will recognize and react to the protein.

There exists antigenic similarity, or cross-reaction, among many grains, and other dietary proteins such as casein with gluten. Based on biological individuality of immune response against a repertoire of gliadin peptides, any number of patients may produce antibodies against a single gluten antigen or a combination of gluten antigens, some of which may be cross-reactive.

A problem with digesting dairy, casein in particular,¹ may be a feature in about 50% of patients with Celiac disease and may, therefore, contribute to persistent symptoms in patients who are on a gluten-free diet.

Gluten-Associated Cross-Reactive Foods can assist the clinician in revealing the possible cause of this continued gluten-like reaction in the patient.

Antibody Array 4

Testing for Gluten-Associated Sensitivity and Cross-Reactive Foods in this array can assist the clinician in revealing the possible cause of this continued gluten-like reaction in the patient. Patients with Gluten-Sensitivity or Celiac disease are sensitized to a **broad range** of dietary proteins, due to enzyme dysfunction, villi damage, or other disorders. **Therefore, it is crucial to identify the food antigens with cross-reactivity to gluten peptides. Without biochemically individualized dietary intervention, the Gluten-Sensitive patient may develop additional autoimmunity.**

Although the majority of individuals with Celiac disease (CD) have substantial improvement within the first few weeks of gluten withdrawal, between 7% and 30% continue to have symptoms or clinical manifestations suggestive of CD despite being on a gluten-free diet.²

Non-responsive Celiac Disease (NRCD) was defined as:

- (1) Referral to a clinician specializing in CD for the evaluation of a lack of response to a gluten-free diet
- (2) Failure of clinical symptoms or laboratory abnormalities typical of CD to improve within 6 months of gluten withdrawal

[Top](#)

- (3) Recurrence of symptoms and/or laboratory abnormalities typical of CD while on a gluten-free diet. Of the 12 identified causes of NRCD, the most common cause was (inadvertent) gluten exposure, accounting for 36% of patients.³ What about the other 64%? An all-too-common contributor to NRCD is cross-reactivity with other foods. Antibody cross-reactivity between different foods or between food and aeroallergens, such as trees and grasses, occurs much more readily than clinically evident cross-reactivity.⁴ The patient often is unable to ‘feel’ the immune response to cross-reactive food.

These are the confusing scenarios when a gluten-sensitive person will say, “What did I eat that was a problem? The packaging didn’t reference any wheat products.” This can be explained in the following:

1. **Consumption of gluten-containing foods such as beer or chewing gum** - Additionally, most countries define “gluten-free” products based on the recommendation of the Food and Agricultural organization of the United Nations and World Health Organization. This codex alimentarius allows the inclusion of up to 0.3% protein from gluten-containing grains in foods labeled “gluten-free.”⁵
2. **Problem with digesting dairy, in particular, casein sensitivity to cow’s milk.** Casein sensitivity may be a feature in about 50% of patients with Celiac disease and may, therefore, contribute to persistent symptoms in Celiac patients who are on a gluten-free diet.^{6 7} Casein also has been suggested as an environmental trigger of other autoimmune disorders such as Behcet’s disease, type-1 diabetes, and systemic lupus erythematosus.^{8 9 10}
3. **Cross-reaction among non-gluten grains, or even infectious agents, and products with gluten.** For example, milk, casein, yeast and many other, as-yet-unidentified, food antigens, salmonella typhi, rotavirus and many other infectious agents, human tissue antigens, such as transglutaminase, heat shock protein, myotubularin-related protein 2 and cell surface receptors (toll-like receptors), all cross-react with gliadin or Celiac peptide.^{11 12 13 14 15} Indeed, bovine milk caseins and transglutaminase-treated cereal prolamins, such as wheat and maize, are differentially recognized by IgA of Celiac disease patients.¹⁶ Studies have identified cross-reactivity among gliadin and foods such as chocolate,¹⁷ sesame,^{18 19 20 21 22} hemp,²³ rye,²⁴ polish wheat,^{25 26} buckwheat,^{27 28 29 30 31 32 33 34 35} sorghum,^{36 37 38 39 40} millet,^{41 42 43 44} spelt,^{45 46 47 48} amaranth,^{49 50 51} quinoa,^{52 53 54} yeast,^{55 56 57 58 59} tapioca,^{60 61 62 63} oats,^{64 65 66 67 68 69} coffee,^{70 71 72 73 74} corn,^{75 76 77} rice,^{78 79 80 81 82} and potato.^{83 84 85}
The response to some of these food allergens parallels the response to gliadin and might be relevant to the pathogenesis of Gluten Sensitivity and Celiac disease by increased mucosal permeability leading to increased antigen resorption, leading to increased immune activation with increased IgA antibodies.⁸⁶ Perhaps this is why as many as 40% of children on a well-managed gluten-free diet for at least 1 year still have elevated antibodies to gluten.⁸⁷

[Top](#)

4. Based on biological individuality and heterogeneity of immune responses, the spectrum of patients elicits a variety of intestinal T-cell responses to a repertoire of gliadin peptides;⁸⁸ and, therefore, any number of patients may produce antibodies against a single antigen or a combination of antigens, which include gliadin, glutenin or agglutinins and their enzymatic digestions in a form of different peptide sizes, 33 MER, 24 MER, 17 MER, 15 MER, gluten exorphin, pro-dynorphin or dynorphins.⁸⁹
5. From these data it is conceivable that patients with Celiac disease are sensitized to a broad range of dietary proteins. Therefore, it is crucial to identify food antigens with a capacity to sensitize patients with Celiac and other autoimmune disorders.^{90 91 92 93}

From the diagnostic and therapeutic point of view, it makes sense to define allergen clusters (cross-reactivity).⁹⁴

Negative serology for transglutaminase, endomysium, or gliadin should not necessarily reassure the clinician⁹⁵ of neither negative immune activation nor pathology from Gluten Sensitivity. Several reports^{96 97 98 99 100} show that in the majority of Celiac patients, these antibodies may be negative or low but cross-reactive antibodies could be elevated.

CLINICAL

When cross-reactivity is present in a patient, gluten antibodies may be essentially normal, and antibodies to the particular antigenic food may be the sole indicator of a continued inflammatory response, triggering the symptomatology of Celiac disease.

Reduced antibodies to gluten—after introduction of a gluten-free diet—probably reflects catabolism of pre-formed antibodies combined with lowered synthesis due to the lack of antigen stimulation. Concurrent reduction of antibodies to other dietary antigens may, therefore, be a better indication of improved mucosal integrity by reflecting decreased penetrability of antigens still available in the gut lumen.

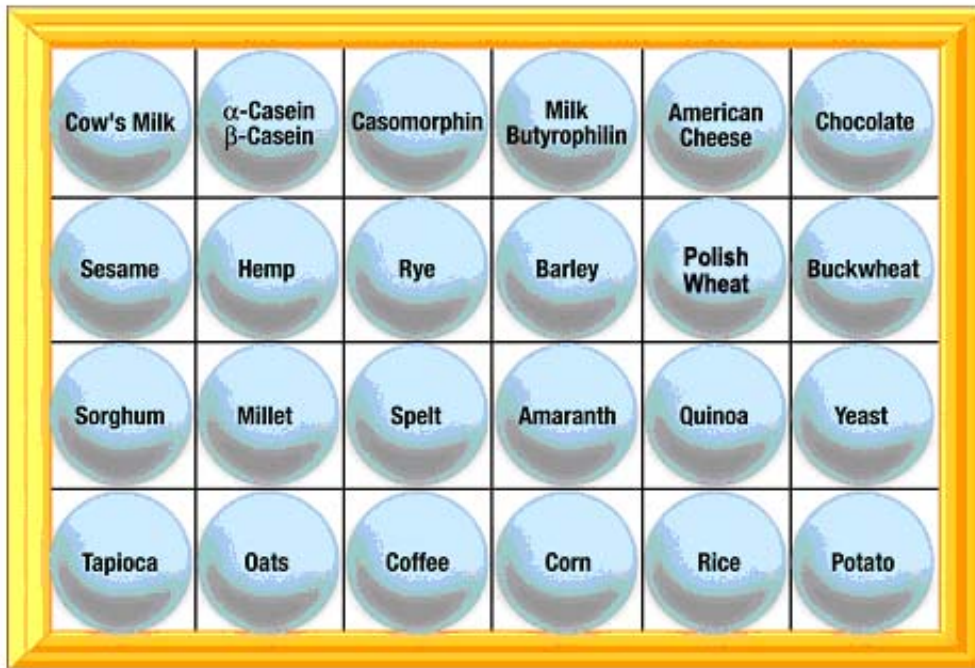
Determination of serum IgA and IgG antibody activities to dietary proteins appears to be a valuable adjunct in the diagnosis and follow-up of diagnosed CD, both in children and adults. Increased IgA activities to other dietary antigens are likewise relatively characteristic of untreated CD; monitoring of such antibodies may be particularly helpful in evaluating the response of patients on a gluten free and cross-reactive diet.¹⁰¹

Therefore, patients with CD or GS suffer an array of autoimmunity beyond the gastrointestinal system. The manifestations and the pathophysiology of CD and GS can be as unique as the individual himself. Identifying these triggers and cascades of autoimmunity is an important step in designing effective treatment and maintenance protocols for the patient.

[Top](#)

Antibody Array 4 – Gluten-Associated Sensitivity and Cross-Reactive Foods

Cyrex Laboratories' Antibody Arrays for Gluten Sensitivity are vital components to the clinical practice. After establishing the patient on a gluten-free diet, many will return after adhering to this diet for months, and yet they still exhibit the same clinical complaints as they experienced with gluten-containing foods. Undoubtedly, these patients are having reactions to foods which cross-react with gluten antigens. Antibody Array 4 – Gluten-Associated Sensitivity and Cross-Reactive Foods is designed to assess these select individuals. With results of this array, the practitioner can take a better, broader approach to developing a tailored diet plan for patients with Celiac disease or gluten sensitivity.



Specimen Requirement

2 mL Serum

Ambient

[Top](#)

Related Testing

Antibody Array 2 – Intestinal Antigenic Permeability Screen (Serum)

[Top](#)

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[Top](#)

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[Top](#)

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[Top](#)

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[Top](#)

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[Top](#)

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[Top](#)

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[Top](#)

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