


# Array 3X – Part 2

Okay, we're going to dive right into talking about some labs.

TEST	RESULT			
	IN RANGE (Normal)	EQUIVOCAL*	OUT OF RANGE	REFERENCE (ELISA Index)
Array 3 – Wheat/Gluten Proteome Reactivity & Autoimmunity				
Wheat IgG			2.12	0.3-1.5
Wheat IgA			2.66	0.1-1.2
Wheat Germ Agglutinin IgG	0.87			0.4-1.3
Wheat Germ Agglutinin IgA	0.48			0.2-1.1
Native & Deamidated Gliadin 33 IgG	0.39			0.2-1.2
Native & Deamidated Gliadin 33 IgA	0.54			0.1-1.1
Alpha Gliadin 17-mer IgG		1.43		0.1-1.5
Alpha Gliadin 17-mer IgA			1.13	0.1-1.1
Gamma Gliadin 15-mer IgG	0.61			0.5-1.5
Gamma Gliadin 15-mer IgA	0.61			0.1-1.0
Omega Gliadin 17-mer IgG	0.71			0.3-1.2
Omega Gliadin 17-mer IgA			2.04	0.1-1.2
Glutenin 21-mer IgG	1.04			0.1-1.5
Glutenin 21-mer IgA			2.33	0.1-1.3
Gluteomorphin + Prodynorphin IgG	0.55			0.3-1.2
Gluteomorphin + Prodynorphin IgA	0.79			0.1-1.2
Gliadin-Transglutaminase Complex IgG	0.42			0.3-1.4
Gliadin-Transglutaminase Complex IgA	0.79			0.2-1.5
Transglutaminase-2 IgG	0.97			0.3-1.6
Transglutaminase-2 IgA	1.09			0.1-1.6
Transglutaminase-3 IgG	0.66			0.2-1.6
Transglutaminase-3 IgA	1.07			0.1-1.5
Transglutaminase-6 IgG	0.83			0.2-1.5
Transglutaminase-6 IgA	0.55			0.1-1.5



**62-year old male**

CC: dizziness, neck pain, heart palpitations, edema

No GI complaints

Suspected gluten intolerance but was not avoiding prior to test

The first patient is a 62-year-old male with chief complaint of dizziness, neck pain, and heart palpitations and edema. And just so you know, the pictures here on these slides are not of the actual patients, they're just something my designer did to add visual interest. Of course we are protecting everyone's privacy here. This patient had no gastrointestinal complaints—this is really, really important, we've already talked about that—and the significance of that is that many patients with gluten intolerance or celiac are missed by both the mainstream medical establishment and also integrative and functional medicine practitioners, because the assumption is that gluten intolerance always comes with gut symptoms, and it's something not true. In this case, this patient did suspect gluten intolerance or that gluten was involved somewhat in his symptoms, but he wasn't avoiding it prior to the test. And as you can see, he was positive for both IgG and IgA antibodies to wheat, and this refers to the entire wheat compound as a whole, not any of the individual components or epitopes of wheat.

# Wheat IgG/IgA

**Associated conditions:** celiac disease, Baker's asthma, dermatitis herpetiformis, gluten-sensitive enteropathy, type 1 diabetes, wheat allergy, wheat-triggered exercise-induced anaphylaxis

Typically **cross-reacts** with rye, barley, and soy

One study showed people **genetically susceptible to T1D** have higher risk of developing when exposed to wheat antigens with pro-inflammatory GI environment

If wheat antibodies elevated, consider **intestinal permeability screen**

So let's take a closer look at what this signifies, antibody production to wheat IgG and IgA. It's associated with celiac disease, baker's asthma, dermatitis herpetiformis, eczema-related conditions, gluten-sensitive enteropathy, some intestinal damage due to gluten, type 1 diabetes, wheat allergy, and wheat-triggered exercise-induced anaphylaxis. When I say associated, I know you know that that means that we haven't necessarily determined a positive relationship in these situations, but you see wheat IgG and IgA antibodies elevated in these other conditions. We also see that wheat typically cross-reacts with rye, barley and soy; we'll be talking more about cross-reactive proteins in Cyrex Array 4. One study showed that people that are genetically susceptible to type 1 diabetes have a higher risk of developing that condition when they're exposed to wheat antigens and also have a pro-inflammatory GI environment, so that's another example of genetic precondition plus the exposome, environmental trigger, in this case wheat and a pro-inflammatory gut environment leading to expression of disease. If wheat antibodies are elevated, consider doing the intestinal permeability screen, which we're going to be talking about.

So, if this patient is negative to celiac and only reacting to wheat and nothing else, it could indicate wheat sensitivity due to poor digestive function, not necessarily gluten intolerance, which is why I suggested an intestinal permeability screen for him. In this case, doing a wheat-free diet, healing his gut and then re-testing might reveal that those antibodies to wheat have declined. However, in this particular instance, you can see that he is reacting to other

components of wheat, not just wheat itself, particularly alpha- and omega-gliadin, and then glutenin.

## Alpha-gliadin

Alpha-gliadin is an **alcohol-soluble glycoprotein**

**Gliadins and glutenins** are the major components of the gluten / protein fraction of the wheat seed

Alpha-gliadin antibodies most likely to be elevated in **CD/NCGS**

Antibodies to gliadin suggest **abnormal mucosal immune response** and intestinal barrier dysfunction

Alpha-gliadin is what most people mean when they're talking about gluten. Gliadin is synonymous with the use of the term gluten. It's an alcohol-soluble glycoprotein, but we need to get more specific about the terminology here. Gliadins and glutenins are the major components of the gluten and protein of the wheat seed, so about half of the protein fraction is made up of gliadin, and the other half is made of gluten. As we've discussed already, alpha-gliadin antibodies are most likely to be elevated in celiac disease and non-celiac gluten sensitivity, so they are important and they are the most likely to be elevated statistically, but not the only ones. Antibodies to alpha-gliadin suggest abnormal mucosal immune response to gluten and intestinal barrier dysfunction.

## Alpha-gliadin

Alpha-gliadin **antibodies** associated with autism spectrum disorders, CD, wheat allergy

Known to **cross-react** with cerebellar proteins (can be confirmed with Cyrex Array 5)

If antibodies to transglutaminase 2 also present, patient most likely has **CD**; should be confirmed with biopsy

If gliadin **positive** but TTG negative, indicates gluten reactivity w/o autoimmunity

Alpha-gliadin antibodies are associated with autism spectrum disorders, celiac disease, and wheat allergy. It's known to cross-react with cerebellar proteins, so these are proteins in the brain, and this can be confirmed with Cyrex Array 5, which you may want to run if patients test positive to any of these epitopes of wheat or gluten on the Cyrex Array 3 panel. Array 5 looks at autoimmune reactivity, so if a patient is reacting to gluten and you suspect that that's causing an autoimmune reaction, Cyrex Array 5 can be helpful. We're not going to cover that in this ADAPT level one course, but we may cover it in future courses. If antibodies to transglutaminase-2 are also present along with alpha-gliadin, the patient likely had celiac disease, and this should be confirmed with the follow-up testing that I mentioned previously. If alpha-gliadin is positive but transglutaminase-2 is negative, it indicates gluten reactivity without a concurrent autoimmune response.

So back to the 62-year-old male case study. This patient was also reacting, as you can see on the slide, to omega-gliadin and glutenin.

## Omega-gliadin

Omega-gliadin is another **epitope of gliadin**

Omega-gliadin **associated with** celiac disease, celiac sprue, exercise-induced anaphylaxis, and wheat allergy

Omega- and gamma-gliadin **antibodies** are not tested for in conventional settings

If your patient only **tests positive** for omega- or gamma-gliadin, but not alpha-, they will be false negative on conventional tests

So omega-gliadin is another epitope of gliadin, and it's associated with celiac disease, celiac sprue, exercise-induced anaphylaxis, and wheat allergy. Omega- and gamma-gliadin antibodies are not tested for in conventional settings, so again if your patient only tests positive for omega- or gamma-gliadin but not alpha-, there'll be false negatives on conventional tests for gluten intolerance.

# Glutenin

Glutenin is the other major fraction of **gluten protein** (with gliadin)

It comprises **47% of the wheat protein**

**Antibodies** IgG and IgA to glutenin are found in patients with celiac disease

**IgA antibodies** to glutenin found in dermatitis herpetiformis

Glutenin is known to **cross-react** with dermal elastin (skin) and rice globulin

Glutenin is the other major fraction of gluten protein along with gliadin. As I mentioned before, it comprises about half, 47 percent, of the wheat protein. IgG and IgA antibodies to glutenin are found in patients with celiac disease, often. IgA antibodies to glutenin are found in patients with dermatitis herpetiformis. Glutenin is known to cross-react with dermal elastin in skin, and also with rice globulin, so a lot of patients who react with gluten will also react to rice.

Okay, moving on to the second study here.

TEST	RESULT			
Array 3 – Wheat/Gluten Proteome Reactivity & Autoimmunity	IN RANGE (Normal)	EQUIVOCAL*	OUT OF RANGE	REFERENCE (ELISA Index)
Wheat IgG		1.27		0.3-1.5
Wheat IgA	0.56			0.1-1.2
Wheat Germ Agglutinin IgG		1.15		0.4-1.3
Wheat Germ Agglutinin IgA	0.55			0.2-1.1
Native & Deamidated Gliadin 33 IgG			1.24	0.2-1.2
Native & Deamidated Gliadin 33 IgA	0.45			0.1-1.1
Alpha Gliadin 17-mer IgG	1.00			0.1-1.5
Alpha Gliadin 17-mer IgA	0.44			0.1-1.1
Gamma Gliadin 15-mer IgG		1.35		0.5-1.5
Gamma Gliadin 15-mer IgA	0.69			0.1-1.0
Omega Gliadin 17-mer IgG	0.64			0.3-1.2
Omega Gliadin 17-mer IgA	0.53			0.1-1.2
Glutenin 21-mer IgG			1.99	0.1-1.5
Glutenin 21-mer IgA	0.61			0.1-1.3
Gluteomorphin + Prodynorphin IgG	0.69			0.3-1.2
Gluteomorphin + Prodynorphin IgA	0.40			0.1-1.2
Gliadin-Transglutaminase Complex IgG	0.59			0.3-1.4
Gliadin-Transglutaminase Complex IgA	0.79			0.2-1.5
Transglutaminase-2 IgG	1.03			0.3-1.6
Transglutaminase-2 IgA	0.34			0.1-1.6
Transglutaminase-3 IgG	1.17			0.2-1.6
Transglutaminase-3 IgA	0.85			0.1-1.5
Transglutaminase-6 IgG	0.93			0.2-1.5
Transglutaminase-6 IgA	0.59			0.1-1.5



**38**-year old female

CC: infertility, endometriosis, digestive issues, acne, overweight

Constipation, abdominal pain, gas, bloating

Vegetarian/vegan and not gluten-free

A 38-year-old female, her chief complaint was infertility, endometriosis, digestive issues, acne, and being overweight. She also had constipation, abdominal pain, gas, and bloating, and she had been until recently following a vegetarian, vegan, and not gluten-free diet. I do get these patients in my practice, believe it or not, even though I'm an advocate of the Paleo type of diet, and wrote a book on that subject, and have a blog and podcast that are oriented around that, you might be surprised at the number of patients I have that are pursuing other dietary paths. And in this case, this woman was eating quite a bit of wheat and gluten still. Three of her antibodies that you can see here are in the equivocal range, she's got equivocal antibodies to IgG wheat, wheat germ agglutinin, IgG, and then gamma-gliadin. Cyrex suggests, and I agree, that most equivocals should be considered as positive in functional medicine. With gluten, the potential effects of undiagnosed and untreated gluten intolerance, I think, are more significant and important than the downside of removing gluten from the diet. If the range is 0.5 to 1.5, and the patient is at 1.35, then to me that's significant to warrant removing gluten, wheat and gluten from the diet, at least for a period of time during the treatment protocol, and then you can always go back and reintroduce and test later, although if you listen to my interview with Dr. Vojdani, who's the scientific advisor for Cyrex and a prominent immunologist, his belief is once you test positive for gluten, you should remove it from your diet entirely. We'll talk a little bit more about that later and also in the Q&As. In addition to wheat and agglutinin as I mentioned, she's also producing out-of-range antibodies to native and deamidated gliadin and wheat germ agglutinin.

## Wheat-germ agglutinin (WGA)

Wheat-germ agglutinin (WGA) is **lectin** (carbohydrate-binding protein) with capacity to **bind multiple cells/ tissue antigens**

WGAs interfere with enzymes and digestive function; also **enhance** antibody production against tissues that it binds (such as islet cells)

**Antibodies** to WGA associated with CD, diabetes, GI disorders, and IgA nephropathy

If WGA antibodies elevated, consider **intestinal permeability screen**

Wheat germ agglutinin is lectin, carbohydrate-binding protein, with capacity to bind multiple cells and tissue antigens, and wheat germ agglutinins interfere with enzymes and digestive function. It can also enhance antibody production against tissues that it binds with, such as islet cells that are involved in insulin production. Antibodies to wheat germ agglutinin are associated with celiac disease, diabetes, gastrointestinal disorders, and IgA nephropathy. If wheat germ agglutinin antibodies are elevated, you should also consider an intestinal permeability screen.



## Deamidated gliadin

Native & deamidated gliadin is produced by **acid or enzymatic treatment of gluten**

**Natural byproduct** of **gluten digestion** in humans; also in processed food (allows gluten to be more easily mixed w/other foods)

Mayo Clinic no longer tests for normal alpha-gliadin because of low sensitivity/specificity; they now test deamidated gliadin instead

**Associated with** CD, autism spectrum disorder, wheat allergy

**Cross-reacts** with numerous tissues and proteins, including myelin basic protein, synapsin, myocardial peptide, dairy products, corn, oats

Native and deamidated gliadin is produced by acid or enzymatic treatment of gluten, so it's a natural byproduct of gluten digestion in humans, but it's also found in processed foods, it's used as an ingredient that allows gluten to be more easily mixed with other foods. The Mayo Clinic, in fact, no longer uses alpha-gliadin as the primary screening test for celiac disease because of its low sensitivity and specificity. They now use deamidated gliadin as the screening test instead. So deamidated gliadin is associated with celiac disease, autism spectrum disorder, and wheat allergy, cross-reacts with numerous tissues and proteins, including myelin basic protein, synapsin, myocardial peptide, dairy products, corn, and oats.

## Deamidated gliadin

Deamidated gliadin **may be huge cause of hidden food intolerance**

**Increasingly** (and extensively) **used as** food emulsifiers, gelling agents, film formation acids, stretching agents in meat products, sauces, soups—and as clarifying agent in red wine

RCTs have shown that even people that don't react to wheat flour can **react to** deamidated gliadin peptides

Most conventional labs **not testing** for it (Mayo and others exception)

Deamidated gliadin may be a huge cause of hidden food intolerances because it is increasingly and extensively used as a food emulsifier, gelling agent, film formation acids, stretching acids in meat products, sauces, and soups, and even as a clarifying agent in red wine. Randomized clinical trials have shown that even people that don't react to wheat flour can react to deamidated gliadin peptides, and the problem is, again, that most conventional labs with Mayo Clinic being a prominent exception are not testing for antibodies to deamidated gliadin.

## Gamma-gliadin

Gamma-gliadin third major **epitope** (along with alpha- and omega-) of gliadin that Cyrex tests for

Suspected to play a significant role in **pathogenesis of CD**

Gamma-gliadin, which this patient was reacting to, is the third major epitope along with alpha- and omega-gliadin that Cyrex tests for, and it is suspected to play a significant role in the pathogenesis of celiac disease.