

Array 3X – Part 4

TEST		R	ESULT		N Contraction
Array 3 – Wheat/Gluten Proteome Reactivity & Autoimmunity	IN RANGE (Normal)	EQUIVOCAL*	OUT OF RANGE	REFERENCE (ELISA Index)	
Wheat IgG		1.50		0.3-1.5	
Wheat IgA	0.66			0.1-1.2	21 -voar old
Wheat Germ Agglutinin IgG			1.66	0.4-1.3	year olu
Wheat Germ Agglutinin IgA	0.53			0.2-1.1	
Native & Deamidated Gliadin 33 IgG	0.73			0.2-1.2	male
Native & Deamidated Gliadin 33 IgA	0.38			0.1-1.1	
Alpha Gliadin 17-mer IgG	0.48			0.1-1.5	
Alpha Gliadin 17-mer IgA	0.33			0.1-1.1	
Gamma Gliadin 15-mer IgG	0.87			0.5-1.5	
Gamma Gliadin 15-mer IgA	0.48			0.1-1.0	CC: constipation
Omega Gliadin 17-mer IgG	0.64			0.3-1.2	neuronathy depression
Omega Gliadin 17-mer IgA	0.41			0.1-1.2	neuropatity, depression
Glutenin 21-mer IgG	0.67			0.1-1.5	
Glutenin 21-mer IgA	0.54			0.1-1.3	Suspected gluter
Gluteomorphin + Prodynorphin IgG	0.33			0.3-1.2	intoloronoo prior to tooting
Gluteomorphin + Prodynorphin IgA	0.45			0.1-1.2	intolerance phor to testing
Gliadin-Transglutaminase Complex IgG		1.18		0.3-1.4	
Gliadin-Transglutaminase Complex IgA	0.66			0.2-1.5	
Transglutaminase-2 IgG	0.85			0.3-1.6	
Transglutaminase-2 IgA	0.54			0.1-1.6	
Transglutaminase-3 IgG	1.12			0.2-1.6	
Transglutaminase-3 IgA	0.60			0.1-1.5	
Transglutaminase-6 IgG			2.41	0.2-1.5	
Transglutaminase-6 IgA	0.62			0.1-1.5	

Okay, next case study, 31-year-old male. Chief complaint was constipation, neuropathy, and depression, and he did suspect gluten intolerance prior to testing. You can see here he's producing equivocal antibodies to wheat, IgG, to gliadin transglutaminase complex IgG, and then out-of-range antibodies to wheat germ agglutinin IgG and then also to transglutaminase 6 IgG, which we haven't talked about in detail yet.

Tissuetransglutaminase 6

tTG-6 primarily expressed in the **brain and neural tissue**

Some research suggests **autoimmunity to tTG-6** results from early brain damage and inflammation

Patients with high tTG-6 antibodies may have **autoimmunity against neuronal tissue**

Associated with cerebral palsy, CD, gluten ataxia, idiopathic spontaneous ataxia, neurodegeneration, peripheral neuropathy



Transglutaminase 6 primarily expresses in the brain and neural tissue. Some research suggests that autoimmunity to tGT 6 results from early brain damage and inflammation. Patients with high tGT 6 antibodies may have autoimmunity against neuronal tissue, and this could explain why with tGT 6 antibodies are associated with cerebral palsy, celiac disease, gluten ataxia, which is a form of paralysis, idiopathic spontaneous ataxia, neurodegeneration, and peripheral neuropathy.

TEST		R	ESULT		
Array 3X - Wheat/Gluten Proteome Reactivity & Autoimmunity	IN RANGE (Normal)	EQUIVOCAL*	OUT OF RANGE	REFERENCE (ELISA Index)	and the second and
Wheat IgG	0.98			0.3-1.5	
Wheat IgA		1.08		0.1-1.2	
Wheat Germ Agglutinin IgG			1.71	0.4-1.3	
Wheat Germ Agglutinin IgA	0.80			0.2-1.1	
Non-Gluten Proteins A IgG	1.24			0.2-2.1	
Non-Gluten Proteins A IgA	1.29			0.2-2.1	
Non-Gluten Proteins B IgG	0.91			0.2-1.9	mal
Non-Gluten Proteins B IgA	1.32			0.2-2.1	man
Gliadin Toxic Peptides IgG	1.32			0.2-1.9	
Gliadin Toxic Peptides IgA		1.36		0.2-1.8	
Native & Deamidated Gliadin 33 IgG	0.90			0.2-1.2	
Native & Deamidated Gliadin 33 IgA	0.64			0.1-1.1	
Alpha Gliadin 17-mer IgG	0.93			0.1-1.5	
Alpha Gliadin 17-mer IgA	0.67			0.1-1.1	CC: Anxiety, ADH
Gamma Gliadin 15-mer IgG	0.95			0.5-1.5	doproceion bair loss and I
Gamma Gliadin 15-mer IgA	0.69			0.1-1.0	uepression nair 1055 and 12
Omega Gliadin 17-mer IgG		0.99		0.3-1.2	
Omega Gliadin 17-mer IgA	0.71			0.1-1.2	
Glutenin 21-mer IgG	1.10			0.1-1.5	Dermatitis, trouble focusing a
Glutenin 21-mer IgA	0.87			0.1-1.3	
Gluteomorphin + Prodynorphin IgG	0.96			0.3-1.2	concentrating at work, brain to
Gluteomorphin + Prodynorphin IgA		0.98		0.1-1.2	J I
Gliadin-Transglutaminase Complex IgG	0.54			0.3-1.4	
Gliadin-Transglutaminase Complex IgA	1.07			0.2-1.5	Standard American di
Microbial Transglutaminase IgG	1.06			0.2-1.8	Stanuaru American di
Microbial Transglutaminase IgA		1.92		0.2-2.3	trouble sticking to a nl
Transglutaminase-2 IgG	0.79			0.3-1.6	trouble sticking to a pro
Transglutaminase-2 IgA	1.00			0.1-1.6	
Transglutaminase-3 IgG		1.53		0.2-1.6	
Transglutaminase-3 IgA	0.66			0.1-1.5	
Transolutaminase-6 IoG	1.10			0.2-1.5	

This was a 26-year-old male. His chief complaint was anxiety, ADHD, depression, hair loss, and IBS. He was experiencing significant mood disturbances, brain fog, and a multitude of skin disorders. Because of antibodies to transglutaminase 3, transglutaminase 6, microbial transglutaminase, and omega gliadin, when he eats wheat and gluten, he will experience symptoms in his brain, nervous system, and skin. If you look at his symptoms, they track perfectly with what we would expect from these markers.



Microbial Transglutami nase

Microbial transglutaminase is **an enzyme produced by bacteria,** which can send signals impacting brain and nervous system function.

It can be exceptionally antigenic in some patients. Patients who consume gluten substitutes like gluten-free pasta may have a reaction to the non-tissue transglutaminase contained within these foods—which may initiate **autoimmune reactivity** against the other transglutaminases.

May send **signals impacting brain and nervous system function,** sometimes contributing to neurological disorders. Also, when found in gluten-free substitutes, may negate the effectiveness of a gluten-free diet in some patients.

Microbial transglutaminase is an enzyme produced by bacteria which can send signals impacting brain and nervous system function. It can be exceptionally antigenic in some patients. Patients who consume gluten substitutes such as gluten-free pasta may have a reaction to the nontissue transglutaminase contained within these foods, which may initiate autoimmune reactivity against the other transglutaminases. Microbial transglutaminase may send signals impacting brain and nervous system function, sometimes contributing to neurological disorders, and when found in gluten-free substitutes, it may negate the effectiveness of a gluten-free diet in some patients, so this is a very important marker, obviously, to screen for and to share with your patients if it is positive.

Once again here, the test results predict the symptoms and complaints, so if you see high antibody production to tGT 6 along with the antibodies to wheat, wheat germ agglutinin, gliadin, and other transglutaminase, they are the gliadin-transglutaminase complex, then you can pretty much expect that that patient will have neurological symptoms or cognitive mood behavior symptoms, and that's exactly what we're seeing here.

Okay, so now that we've covered all of the markers that are on this panel, let's look at some more labs. You are more familiar with the markers now, so it should be easier for us to go through these labs.



Here's a 52-year-old female. Chief complaint is loose stools, gas, bloating, fatigue, weight gain, and hormone imbalance, and this is a good example of what celiac disease can look like on a Cyrex Array 3 panel.

TEST		R	ESULT		
Array 3 – Wheat/Gluten Proteome Reactivity & Autoimmunity	IN RANGE (Normal)	EQUIVOCAL*	OUT OF RANGE	REFERENCE (ELISA Index)	
Wheat IgG	0.44			0.3-1.5	
Wheat IgA		0.96		0.1-1.2	52 -voar old
Wheat Germ Agglutinin IgG	0.95			0.4-1.3	year old
Wheat Germ Agglutinin IgA	0.72			0.2-1.1	
Native & Deamidated Gliadin 33 IgG	0.49			0.2-1.2	temale
Native & Deamidated Gliadin 33 IgA	0.79			0.1-1.1	
Alpha Gliadin 17-mer IgG		1.13		0.1-1.5	
Alpha Gliadin 17-mer IgA		1.00		0.1-1.1	
Gamma Gliadin 15-mer IgG		1.32		0.5-1.5	CC: loose stools, gas bloating, fatigue, weigh oain, hormone imbalanc
Gamma Gliadin 15-mer IgA	0.73			0.1-1.0	
Omega Gliadin 17-mer IgG		1.03		0.3-1.2	
Omega Gliadin 17-mer IgA		1.00		0.1-1.2	
Glutenin 21-mer IgG			1.51	0.1-1.5	3 ,
Glutenin 21-mer IgA	0.81			0.1-1.3	
Gluteomorphin + Prodynorphin IgG			1.49	0.3-1.2	Follow-up testing
Gluteomorphin + Prodynorphin IgA	0.87			0.1-1.2	
Gliadin-Transglutaminase Complex IgG	0.59			0.3-1.4	revealed CL
Gliadin-Transglutaminase Complex IgA	0.78			0.2-1.5	
Transglutaminase-2 IgG			1.63	0.3-1.6	
Transglutaminase-2 IgA	0.88			0.1-1.6	
Transglutaminase-3 IgG	1.02			0.2-1.6	
Transglutaminase-3 IgA	0.91			0.1-1.5	
Transglutaminase-6 IgG		1.25		0.2-1.5	
Transolutaminase-6 lgA		1.14		0.1-1.5	

We see that the alpha gliadin antibodies, both IgG and IgA, were equivocal, but they were elevated, and then you can see that transglutaminase 2 was outside of the lab range, not significantly, but it was elevated. Then she has an array of antibodies to other epitopes and also to transglutaminase 6. With the positive alpha gliadin and transglutaminase 2, we did some additional testing, and then I eventually referred her out to a gastroenterologist. She did have a positive biopsy and was diagnosed at 52 years old with celiac disease, so she very likely had this for years if not decades and was just finding out about it at 52 years old.



Next is a 37-year-old male. Chief complaints were issues with sleep, blood sugar, hyperlipidemia, high cholesterol, and being overweight.

TEST		RI	ESULT		
Array 3 – Wheat/Gluten Proteome Reactivity & Autoimmunity	IN RANGE (Normal)	EQUIVOCAL*	OUT OF RANGE	REFERENCE (ELISA Index)	
Wheat IgG	1.03			0.3-1.5	
Wheat IgA			1.30	0.1-1.2	27 -Voar old
Wheat Germ Agglutinin IgG	0.93			0.4-1.3	year olu
Wheat Germ Agglutinin IgA			1.31	0.2-1.1	
Native & Deamidated Gliadin 33 IgG			2.26	0.2-1.2	male
Native & Deamidated Gliadin 33 IgA			1.36	0.1-1.1	mare
Alpha Gliadin 17-mer IgG	0.61			0.1-1.5	
Alpha Gliadin 17-mer IgA	0.87			0.1-1.1	
Gamma Gliadin 15-mer IgG	0.55			0.5-1.5	
Gamma Gliadin 15-mer IgA	0.72			0.1-1.0	CC: sleep, blood suga
Omega Gliadin 17-mer IgG			1.41	0.3-1.2	cholesterol overweigh
Omega Gliadin 17-mer IgA			1.55	0.1-1.2	cholesterol, overweigt
Glutenin 21-mer IgG	0.73			0.1-1.5	
Glutenin 21-mer IgA		1.20		0.1-1.3	No digestive complaint
Gluteomorphin + Prodynorphin IgG	0.58			0.3-1.2	no digestive complaint
Gluteomorphin + Prodynorphin IgA		1.15		0.1-1.2	
Gliadin-Transglutaminase Complex IgG	0.74			0.3-1.4	Follow-up testing
Gliadin-Transglutaminase Complex IgA	0.93			0.2-1.5	
Transglutaminase-2 IgG	0.59			0.3-1.6	revealed "silent" Cl
Transglutaminase-2 IgA		1.27		0.1-1.6	
Transglutaminase-3 IgG	0.47			0.2-1.6	
Transglutaminase-3 IgA	0.72			0.1-1.5	
Transglutaminase-6 IgG	0.71			0.2-1.5	
Transglutaminase-6 IgA		1.31		0.1-1.5	

This man did not have any digestive complaints, but as you can see here, he was positive for numerous antibodies to wheat antigens or epitopes of wheat here on Cyrex Array 3. He was clearly reacting to wheat, but he was not positive to the two main antibodies used to screen for celiac disease. He was equivocal for transglutaminase 2 IgA antibodies, but that would show up as normal on a conventional test because it's just more binary. It's either normal or not normal. They don't have the equivocal range, and he was negative for antibodies to alpha-gliadin.

However, you can see that he had strongly positive antibodies to native and deamidated gliadin, IgG and IgA, and this is perhaps one reason why the Mayo Clinic is now using this in preference to alpha gliadin because they find that it is more sensitive and specific. He was also producing antibodies to omega gliadin. I ended up sending him out to the gastroenterologist for additional screening because the patient was very resistant to cutting out gluten entirely from his diet, and I suspected that he may have celiac disease, and it turned out that he did.

This is tricky because it's not an obvious case of celiac here with alpha gliadin and transglutaminase 2, but we have strong antibody production to deamidated gliadin, which as I mentioned is arguably more sensitive and specific for celiac, and then we had antibody production to transglutaminase 2 in a patient who was not wanting to remove gluten from his diet and didn't really take it seriously enough, I think. Once he did get the diagnosis for celiac disease, he did take it seriously and did remove gluten from his diet. This a form of celiac known as silent celiac disease, which manifests without the typical enteropathy or without the typical



gut symptoms such as diarrhea, gas, bloating, and strong gastrointestinal reaction when gluten is consumed.

"Silent" celiac disease

Several studies show that the **majority** of **CD patients** don't test positive for antibodies to alpha-gliadin or transglutaminase-2

Especially true when **GI enteropathy** is mild

Some studies suggest **sensitivity** as low as 27-31% (with alpha-gliadin and TTG2) when villous atrophy is mild

1 in 2 new patients diagnosed with CD doesn't have gut symptoms

For every 1 case of diagnosed CD, there are **6.4 cases undiagnosed**

A little more on silent celiac disease. Several studies show that the majority of celiac disease patients don't test positive for antibodies to alpha gliadin or transglutaminase 2, so again, this makes diagnosis of it difficult and challenging, and it explains why it is so underdiagnosed. This is especially true when the GI enteropathy is mild, meaning if there is not a lot of intestinal damage, the patients are less likely to test positive for alpha gliadin or transglutaminase 2 antibodies. Some studies suggest that sensitivity of alpha gliadin and transglutaminase is as low as 27 to 31 percent when villous atrophy is mild. In other words, if there isn't much intestinal damage, only 27 to 31 percent of patients with celiac will test positive for that combination of alpha gliadin and transglutaminase 2 antibodies.

One in two new patients who are diagnosed with celiac disease don't have gut symptoms. I'm just going to say that again: one in two new patients diagnosed with celiac don't have gut symptoms. I think that would shock a lot of doctors and patients, so it's a really important statistic to have at the tip of your tongue. Here's another one that's really kind of tragic actually. For every one diagnosed case of celiac disease, there are 6.4 cases that are undiagnosed.



"Silent" celiac disease

Silent CD every bit **as harmful as obvious CD** (possibly more, since unrecognized)

It's **associated with** 4-fold increase in mortality, as well as numerous chronic, inflammatory conditions

Affects skin (dermatitis herpetiformis, psoriatic arthritis), brain (gluten ataxia, schizophrenia, idiopathic neuropathies), endocrine system (diabetes, nephritis), metabolism (overweight/obesity) and more

Reason CD so often missed: tests rely only on alpha-gliadin and TTG2 antibodies

Silent celiac disease is, unfortunately, is every bit as harmful as the more obvious form of celiac disease, and I would argue that it's probably more harmful because it's more likely to go unrecognized and be undiagnosed for a longer period of time. It's associated with a fourfold increase in mortality as well as numerous chronic inflammatory conditions. It affects the skin, conditions such as dermatitis herpetiformis or psoriatic arthritis; the brain by gluten ataxia, schizophrenia, idiopathic neuropathies; the endocrine system, conditions such as diabetes and nephritis; metabolism, overweight and obesity, and more. Again, the reason that celiac disease is so often missed is those conventional tests relying only on alpha gliadin and tGT 2 antibodies, which as we just reviewed, can be only 25 to 27 percent sensitive in people who don't have significant enteropathy.