

# Cyrex Array 4 – Part 1

Hey, everybody, this week we're going to talk about testing for cross-reactive protein intolerance and other food sensitivities with Cyrex Array 4. Several studies show that between 7 and 30 percent of people with celiac disease continue to have symptoms even after implementing a gluten-free diet. We also know that up to 50 percent of people with celiac disease react to casein, which is a protein in dairy products. So the theory is, there is antigenic similarity across proteins in dairy, grains, eggs, and other foods, and some antibodies to gluten may cross-react with these other food antigens. A lot of patients that are diagnosed with celiac disease and non-celiac gluten sensitivity turn to gluten-free alternatives, like gluten-free breads or pastas, all kinds of other processed or at least somewhat processed foods made with rice, corn, tapioca, quinoa, teff, et cetera. The problem is, if they're also producing antibodies to these foods, it may improve somewhat, but they're not going to completely get better, and that's where the Cyrex Array 4 can come in handy.



## Who should get tested with Array 4?

- 1 Anyone that still **experience symptoms after gluten-free diet** (whether they have CD or NCGS)
- 2 Anyone who **wants to be able to consume the foods on Array 4**, and needs clarity on how they are affected by them

So who should you run Cyrex Array 4 on? Our current approach is that we will run it with anyone that still experiences symptoms after adopting a gluten-free diet, whether they have celiac disease or non-celiac gluten sensitivity, and also anyone who wants to be able to consume the foods on Array 4 and needs clarity on how they're affected by them.



# Test Preparation

(Important!)

- 1 Exposure to **particular foods** is what triggers antibody production
- 2 Patient must have consumed each food on Array 4 **within 25-30 days** of test for accurate results
- 3 Advise patient to eat **at least one small serving of each food they wish to test** for minimum of 7 days, starting 25-30 days before test
- 4 If patient has known gluten intolerance, instruct them to **avoid barley, Polish wheat (kamut), rye, spelt, and oats** (if not certified gluten-free)
- 5 **Two options:** have patient consume all foods (difficult), or only those they wish to test/are currently consuming

So, there are some really important things that your patients need to be aware of in terms of preparing for the test, in order to get an accurate result. I've listed them here on the slide. We've also provided a patient handout describing this process in detail that you can generate with the handout generator.

So, exposure to particular foods is what triggers antibody production in the first place, and that's how these tests work. So in order to get a positive result on any of the antigens on the panel, the patient must have consumed each of them on the panel within 25 to 30 days of the test. So what we will typically do is advise patients to eat at least one small serving of each food that they wish to test for a minimum of seven days starting about 25 to 30 days before the test. So that language was specific, at least one small serving of each food they wish to test.

There are some proteins or foods on this panel that your patient might not care about at all, like teff, for example, not a lot of people eat it. It does tend to show up in some of the gluten-free cereals and baked products and processed foods, but if your patient isn't eating any of those, they don't even know what teff is, and they don't have any desire to eat teff, then they don't necessarily have to include it in this pre-test protocol. They probably won't see any antibody production against it, and that could be a false negative, but again that doesn't matter if they don't have any intention of eating it. If a patient has known gluten intolerance, you would instruct them to avoid barley; Polish wheat, which is also called kamut; rye; spelt; and oats, if the oats are not certified gluten-free. So if you've already done the Cyrex Array 3 and you know that they're gluten-intolerant, there's no reason to put them through the pain of eating those foods just to find out what you already know with this test.

And so, the options for how to do this in practice would be to have the patient consume all of the different foods, which can be difficult. There are definitely some breakfast cereals that are made that have a number of these antigens' foods present in them, and if the patient really makes an effort they can do it, or as I said before, the patient can only consume the ones that they want to test, or just that are part of their normal diet. In other words, they wouldn't make any changes and they would just continue to eat what they're eating, assuming they're eating the foods that are tested and they see what turns up. So there are different approaches depending on the patient and their goals and desires.

So let's dive right into looking at some test results.

TEST	RESULT			REFERENCE (ELISA Index)
	IN RANGE (Normal)	EQUIVOCAL*	OUT OF RANGE	
<b>Array 4 – Gluten-Associated Cross-Reactive Foods and Foods Sensitivity **</b>				
Rye, Barley, Spelt, Polish Wheat		1.33		0.4-1.4
Cow's Milk	0.84			0.1-1.3
Casein (Alpha & Beta)	0.93			0.1-1.7
Casomorphin	0.98			0.2-1.6
Milk Butyrophilin	1.35			0.2-1.8
Whey Protein	0.70			0.1-1.3
Chocolate (Milk)	0.75			0.1-1.4
Oats	0.40			0.2-1.0
Yeast		1.10		0.2-1.2
Coffee	1.05			0.3-1.9
Sesame	0.92			0.1-1.3
Buckwheat			3.07	0.4-1.3
Sorghum	0.66			0.3-1.2
Millet	0.71			0.3-1.5
Hemp	0.64			0.3-1.5
Amaranth	0.50			0.2-1.3
Quinoa	0.72			0.5-1.5
Tapioca	0.30			0.1-1.1
Teff	0.40			0.2-1.1
Soy	0.55			0.5-1.5
Egg	0.70			0.2-1.7
Corn	0.53			0.3-1.4
Rice	0.99			0.4-1.6
Potato	0.79			0.6-1.4

## Rye, barley, spelt, kamut

Gluten-containing **grains**

**Associated with** allergy, asthma, CD, ME/CFS, fibromyalgia, IBS, NCGS

**Cross-reacts** with Sesame seed, w-gliadin, and wheat, barley and soy flours

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Oats	0.40			0.2-1.0
Yeast		1.10		0.2-1.2
Coffee	1.05			0.3-1.9
Sesame	0.92			0.1-1.3
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Sorghum	0.66			0.3-1.2
Millet	0.71			0.3-1.5
Hemp	0.64			0.3-1.5
Amaranth	0.50			0.2-1.3
Quinoa	0.72			0.5-1.5
Tapioca	0.30			0.1-1.1
Teff	0.40			0.2-1.1
Soy	0.55			0.5-1.5
Egg	0.70			0.2-1.7
Corn	0.53			0.3-1.4
Rice	0.99			0.4-1.6
Potato	0.79			0.6-1.4

The interpretation of Cyrex Array 4 is a lot more straightforward than Cyrex Array 3, the gluten wheat proteanome panel that we just covered. Mostly, it's "what you see is what you get," but we're going to go through and talk about some specific considerations for each group. This test shows equivocal positive to rye, barley, spelt, kamut, these are gluten-containing grains, and their intolerance to this set of grains is associated with allergy, asthma, celiac disease, ME/CFS, which is the provisional term for chronic fatigue syndrome now, fibromyalgia, irritable bowel syndrome, and non-celiac gluten sensitivity. And patients that tend to react to this also tend to react to sesame seed, various forms of gliadin, wheat, barley, and soy flour.



## Yeast

### **Saccharomyces cerevisiae:**

yeast used as a leavening agent in baking and as a fermenting agent in brewing

**Associated with** Crohn's disease, IBD, tropomyositis, Behçet's disease

**Cross-reacts** with *Candida albicans*, multiple bacteria, human colon tissue, gliadin

Patients with **antibodies** to yeast should be screened for intestinal permeability

There were also antibodies on the last test result there to yeast, so the particular yeast that they're testing for in Cyrex is *saccharomyces cerevisiae*, so this is a yeast used as a leavening agent in baking and also as a fermenting agent in brewing, like with beer. So the antibodies to this type of yeast are associated with Crohn's disease and ulcerative colitis, tropomyosin, and Behçet's disease. It cross-reacts with *candida albicans*, another yeast; multiple species of bacteria; human colon tissue; and gluten, and patients with antibodies to yeast should be screened for intestinal permeability because those conditions will often occur together.



A **seed** used in Japanese noodles, porridge, pancakes, and farina

**Gluten-free**, but some studies show antigenicity with patients with CD and NCGS

**Associated with** CD, urticaria, NCGS, allergy, and asthma

**Cross-reacts** with latex; patients with buckwheat reactivity should avoid latex products

There are also antibodies to buckwheat on that result. Buckwheat is a seed actually, not a grain; it's used in Japanese noodles, porridge, pancakes, and farina. It's gluten-free, but some studies show antigenicity with patients with celiac disease and non-celiac gluten sensitivity. It's associated with celiac disease, urticaria, non-celiac gluten sensitivity, allergy, and asthma, and it cross-reacts with latex, so patients with reactivity to buckwheat should avoid using any products with latex.

Okay, so here's another test result.

# Milk butyrophilin

**Protein** of the milk fat globule membrane

**Associated with** MS, Sjögren's, lupus

**Cross-reacts** with myelin oligodendrocyte glycoprotein and gliadin

**Can provoke** immune responses in GALT and peripheral immune organs

**Exacerbates** central nervous system inflammation

TEST	RESULT			
Array 4 – Gluten-Associated Cross-Reactive Foods and Foods Sensitivity **	IN RANGE (Normal)	EQUIVOCAL*	OUT OF RANGE	REFERENCE (ELISA Index)
Rye, Barley, Spelt, Polish Wheat	0.59			0.4-1.4
Cow's Milk	0.74			0.1-1.3
Casein (Alpha & Beta)	1.02			0.1-1.7
Casomorphin	1.00			0.2-1.6
Milk Butyrophilin			3.37	0.2-1.8
Whey Protein	0.86			0.1-1.3
Chocolate (Milk)	0.70			0.1-1.4
Oats		0.92		0.2-1.0
Yeast			1.61	0.2-1.2
Coffee		1.60		0.3-1.9
Sesame	0.77			0.1-1.3
Buckwheat	0.63			0.4-1.3
Sorghum	0.57			0.3-1.2
Millet	0.90			0.3-1.5
Hemp	0.94			0.3-1.5
Amaranth	0.60			0.2-1.3
Quinoa	0.87			0.5-1.5
Tapioca	0.76			0.1-1.1
Teff		1.07		0.2-1.1
Soy	0.66			0.5-1.5
Egg	0.78			0.2-1.7
Corn	0.70			0.3-1.4
Rice	0.92			0.4-1.6
Potato		1.27		0.6-1.4

As you can see, this patient is reacting to multiple antigens. Let's start with milk butyrophilin. This is a protein of the milk fat globule membrane, and it's associated with multiple sclerosis, Sjögren's, and lupus; cross-reacts with myelin oligodendrocyte glycoprotein, which probably explains the MS association; and gluten. It can provoke immune responses in the gut-associated lymphoid tissue, or GALT, and in peripheral immune organs, and it exacerbates central nervous system inflammation.



Oats **do not contain gluten** unless cross-contaminated

**Associated with** atopic dermatitis, CD, food hypersensitivity, NCGS

**Cross-reacts** with gliadin

The patient is also reacting to oats. Oats don't contain gluten unless they're cross-contaminated, which unfortunately they often are. So, oats are typically produced in the same kind of factories that produce gluten-containing products, so unless oats specifically say that they're gluten-free on the package, you should assume and tell your patients to assume that they contain gluten. Antibodies to oats are associated with atopic dermatitis, celiac disease, food hypersensitivity, and non-celiac gluten sensitivity, and there's also cross-reactivity with gluten.