A Grain of Truth: The Gluten Summit
Presenter: Aristo Vojdani

Properly Testing for Gluten Sensitivity and Why Current Methods Fail

Dr. O'Bryan: Well, hello, everyone! Welcome to another edition of A Grain of Truth: The Gluten eSummit. And it is my privilege and honor to be interviewing one of the world's greats today, Dr. Aristo Vojdani. Dr. Vojdani's research spanning a 40-year career focuses on the role of environment and environmental factors, such as toxic chemicals, infections, dietary proteins, and peptides in complex diseases, so how mercury or aluminum might be affecting our brain, how food sensitivity such as gluten might be affecting us in complex diseases.

Dr. Vojdani obtained his PhD in Immunology and Microbiology and carried out post-doctoral studies in Comparative Immunology at UCLA, and Cellular Immunology at Tel Aviv University Medical Center. Dr. Vojdani is CEO and Technical Director of Immunosciences Lab, and Chief Scientific Advisor at Cyrex Laboratories.

Dr. Vojdani has published over 120 peer-reviewed articles in scientific journals. He's a member of the editorial board, meaning he reviews other people's research before it's published, of the following peer-reviewed journals: the *Journal of Toxicology and Industrial Health*, the *Journal of Environmental Epidemiology and Toxicology*, the *European Journal of Inflammation*, and *Evidence-Based Complementary and Alternative Medicine*.

In 1984 he was the recipient of the Scientific Presentation Award from the American Academy of Otolaryngic Allergy. He has participated in research which has been funded by the Environmental Protection Agency, the National Institute of Health, the National Institute of Allergy and Infectious Diseases, and the Department of Veterans Affairs.

And on a personal note, he is my good friend and my mentor in understanding the role of the immune system in our health.

Dr. Vojdani, thank you so much for joining us today!

Dr. Vojdani: I am very honored to be interviewed by my friend, Dr. Tom O'Bryan!

Dr. O'Bryan: Thank you, thank you. Dr. Vojdani, to start with you are an immunologist. That's a scientist who studies the immune system and the role it plays in our health.

Can you tell us in language that the general **[2:30]** public understands, what is the purpose of our immune system?

Dr. Vojdani: I will explain to you. But also I will tell you why you are taking me back to almost 40 years ago when I was taking my first course in immunology. So we have the immune system in order to have protection against the environment which we are living in. I mean, the environment could be whatever is in the environment, it could be bacteria, virus, parasites, dietary proteins and peptides, and many other factors, and even toxic chemicals.

So, you took me back to almost 40-45 years ago when, at the end of the course of immunology, the professor asked us exactly that question. “What is the purpose of the immune system? Write two pages about the purpose of the immune system.” My answer was that the immune system is like a policeman. The policeman which is protecting the community against any invasion. And when the policeman sleeps on the job, as you know, the end result of that will be immune invasion, immune deficiency, autoimmune disease and many other associated disorders. So we have the immune system in order to protect us against any foreign invasion.

Dr. O’Bryan: Thank you. That’s a wonderful answer. And it validates what I also have been saying. I tell patients and in our lectures that the immune system is the Armed Forces in our body. There’s an Army, an Air Force, a Marine, a Coast Guard, a Navy, IgG, IgA, IgE, IgM. There’s different branches of the immune system. One of the questions that doctors often are asked or doctors themselves will ask in **[5:00]** is, “Which test should I do looking for an immune reaction?” And we have this idea as doctors that there’s one test that’s going to be accurate.

But is it not true that the Army may not be called out—IgG—and perhaps it’s the Navy that’s called out—IgA?

Dr. Vojdani: Absolutely, absolutely! Dr. O’Bryan, not only that, it’s not just the antibodies. You’ve already very elegantly explained different arms of the immune system. We have cellular immunity, meaning the cells, by producing all kinds of need-meeters, such as cytokines, chemokines, without production of antibodies. Sometimes chemokines and cytokines can protect us against foreign material. And we call that the cellular arm of the immune system.

On the other hand, we have the humoral arm of the immune system, meaning cells reacting to the foreign material, and they produce IgG, IgM, IgA, IgE. So by looking just on IgG, it’s not enough. You are going to miss, probably, all the immune reactions associated with IgE, which is allergy, or IgM, or IgA. So unless you look at all of the antibodies, the cytokines, the cellular immune reactions, natural killer cell activity, T cell

function, B cell function, the subpopulation of the lymphocytes, as you know, such as Th1, Th2, Th3, Th17, and follicular T helper cells.

So again, this goes back to your definition of the immune system, different arms of the immune system. Unless we look at all of that, we are going to miss major components of the abnormalities which we are looking for.

Dr. O'Bryan: This is a critical concept for our audience to understand. This is one of the foundational concepts. **[7:30]** It's my goal that everyone has a basic understanding of coming through listening to these 29 hours of interviews with world experts. The concept is that if you're checking one branch of the immune system, for example IgE--and that is the skin prick test that most people are familiar with--the studies show us that forty-plus percent of children and over fifty percent of adults will come back falsely negative on a skin prick test, meaning that the test comes back negative, but they really have a problem with that substance that's being tested. It comes back falsely negative. And that's because the Army is not being called out, it's the Navy that's being called out.

So we must have this wider overview of testing to see what might be a problem for us. And this is for our listening audience. This is a critical concept to understand. When you take your child to the allergist, some allergists and general practitioners will know that they have to look from many different angles. And some will be thinking, "Just checking the pin prick test is enough by itself."

Dr. Vojdani, are there examples when a patient goes to a doctor for a test of their immune system to see what environmental triggers might be harming them, and if the doctor does one test and it comes back negative, saying there's no problem, is there ever a time that we can rest comfortably knowing that that's going to be completely accurate?

Dr. Vojdani: Thank you for asking this question, and also the comment you made earlier about prick tests. The prick test particularly has many false negatives when the allergist tests for food allergy, when they test, for example, skin testing for milk, soy, corn. Unfortunately, their prick test with food antigens, it has many false negatives, sometimes even false positives. **[10:00]** The false negatives are based on the fact that we do not have determinations for exact allergens causing allergy in the patient. So what they do, they take extracts of food and inject into the skin. And if that extract is made, for example, in acetone or alcohol, the patient may react to alcohol, and that will result in a false positive report.

On the other hand, because there are so many mixtures of antigens injected into the skin, they may get false positive results. That's why, in relation to food sensitivity, and allergy in this case, in vitro testing, meaning testing blood in a laboratory setting and

looking for IgE antibodies against various food antigens is more accurate than skin testing. The skin testing is very good for inhalant allergens or other environmentals. So particularly there are some false positives and false negatives in relation to foods if we measure only IgE.

Furthermore, we know that immune reaction or immune abnormalities, it's not only IgE-mediated. What if the patient is eating something today, not reacting to that immediately like in relation to IgE response, like five minutes later, a few seconds later, or a couple of hours later. But some individuals can eat something today and will have a delayed immune reaction, which could be cellular-mediated, meaning lymphocytes will react to that food in the body and become activated, release cytokines, and then those are the mediators causing abnormal symptomatology.

Or what if the patient is going to produce IgG? Or produce IgM or IgA against certain foods? So therefore, if we do not measure all these antibodies—including IgG, **[12:30]** IgM, IgA, and IgE—against some of these environmental factors, in particular, food antigens, then we are going to miss a significant percentage of patients who may have sensitivities to some of these environmental factors.

Dr. O'Bryan: That was a brilliant overview. And I want to review three points from that for our doctors and health care practitioners listening to this, and for our mothers of children trying to figure out what's wrong with their kids and looking for an allergic response.

Three things: one, IgE, which is the reaction that can be very dangerous when we hear about peanut allergies and being unable to breathe with exposure, that's an IgE reaction. Sometimes it can come back with false negatives or false positives. And the way to reduce the number of false negatives or false positives is to do the blood test looking for the IgE antibodies versus the skin prick test. Would that be correct, Dr. Vojdani?

Dr. Vojdani: Yes, absolutely!

Dr. O'Bryan: Okay. And another point to that is that the skin prick test, when was that test first developed?

Dr. Vojdani: Almost 120 years ago.

Dr. O'Bryan: That's my point is that it's almost 120 years old. It's a good test, it can be used. From my experience, if it comes back positive it's likely positive. But there may be a false positive because of the carrier substance like alcohol. But it can come back with false negatives. So the technology has improved. And what we now know is that a

blood test for IgE—for the Air Force, if IgE is the Air Force—the blood test is more sensitive. You're going to find more of the people that are having the Air Force called out in IgE reaction if you do a blood test. So if your doctor is an allergist and they do IgE testing, ask for a blood test. They may want to do the skin prick test, but ask for a blood test to go along with it so that you can get confirmation.

Would that be a rational approach, Dr. Vojdani?

Dr. Vojdani: With no doubt. And also I would like to add one more item to some of these problems. As you know, **[15:00]** there are many laboratories or many companies [that] make extracts of allergens—ragweed, house dust mites, milk, soy, corn, meat, and so forth. In the majority of the cases, probably 99% of these companies, they make, in relation to foods I'm talking about, extracts from raw food. And so my question is, "What percentage of the population is going to eat raw meat that we are testing allergy for raw meat?"

And that's why a couple of years ago—I'm sure you have seen my article—that I did a comparison between raw foods versus modified foods or cooked foods, and found that some people, as you know, do not react to raw foods. They may react to modified or cooked foods. So the conclusion is that this is another reason that when we do skin testing we may get false negative results. So let's not just blame everything on skin testing. Laboratories who are using raw foods in their antibody testing—which I know the majority of them are using raw foods because they buy them from those companies—they may get false negative results. So they have their own share of problems with their testing.

Dr. O'Bryan: This is a critical concept for our practitioners. This is a critical concept of the difference between cooked and raw. So that's another example of why one particular test by itself cannot be comprehensive enough to get an accurate measure for us.

Now, I said there were three things I wanted to review that you had just spoken of, Dr. Vojdani. The first one was the IgE skin prick versus the blood, and how critically important that is for our health care practitioners.

The second one is that sometimes there is a delayed immune reaction. So doing a skin prick **[17:30]** when you prick the skin with the food substance or grasses or whatever, it may not react. And we know, of course, that if it's an autoimmune mechanism—so it's activating their antibodies to the food—that that can have an 8-day delay before the patients will have symptoms. So they have an exposure. Some people will react quickly to that exposure. But some people won't react for up to 8 days. Is that because the

immune system has to get turned back on? And it starts producing the antibodies, and it takes a while for those antibodies to rise in the bloodstream?

Dr. Vojdani: Yes, definitely. For example, in the case of IgE-mediated reaction, why it is immediate is because there is IgE in circulation. [It] immediately binds the antigen. And the whole IgE plus antigen binds to the receptor on different cells, which releases the mediators and immediately—within minutes or hours—the child will have reaction to peanuts, for example.

Dr. O'Bryan: Yes.

Dr. Vojdani: But if another child is having a delayed reaction to peanuts or milk or wheat or corn, that antigen has to go through a different process, and the production of IgG sometimes takes one week, sometimes takes two weeks. So, therefore, the delayed reaction occurs three days later, a week later, two weeks later. So therefore it's very difficult to find out what was the cause?

In a case of IgE-mediated response, sometimes people don't need a blood test because if you eat peanuts, immediately you're going to have a reaction and can find out that really you have allergic reaction to peanuts. But if you eat something today and one week later or 6 days later or ten days later, you are going to have an IgG or IgM or IgA immune response, there is no way that you are going to find out which food was the cause of this IgG or IgA or IgM production.

Dr. O'Bryan: I want to say to our listening audience, I'm sorry **[20:00]** if this is a little bit on the technical side. But this is so critical to understanding, identifying, what the environmental trigger is that's affecting you and your children. This is one that you're going to want to listen to a couple of times and take notes so that you can form your questions properly when you go back to your own doctor, your own clinician, and ask for a more comprehensive test, in some cases.

Dr. Vojdani: Dr. O'Bryan, allow me to give you another simple example that the listeners will learn more about it. Let's take example of a sausage or hotdog. Okay? So we have protein, they add some gluten to that to make it sticky, and they add lots of preservatives, maybe some spices. And to me that's the major, major ingredients. So I have seen or I have tested many blood tests, blood samples. I have tested many blood samples that they did not react separately. When we tested that blood against wheat, it was negative. Against meat, it was negative. But when I extracted the antigens from the hotdog or sausage, they reacted to hotdog and sausage.

So what's happening here? Meaning, by modifying the food through cooking, through adding preservatives, let's not forget that also the preservatives themselves can bind to

the proteins and make them more antigenic, and so therefore our immune system is going to react to those much stronger and will produce a lot of IgG, or IgA or IgM, or IgE.

So that's another example that some individuals may not react to major ingredients of certain foods we are consuming. But when we consume the end product, such as sausage or **[22:30]** hotdog, then we are going to have immune reaction to whatever is in that end product, we call it sausage or hotdog.

Dr. O'Bryan: This is a very important concept. And I'm sure those that have been following this conversation so far are now thinking, "Oh, my goodness! Well how can I test anything and be certain about the results?" And in some cases, that's really the takeaway is that our science is not as sophisticated as we would like it to be. And by testing beef or testing turmeric or testing the casing material of a sausage, it may come back negative. But the combined product and what happens in the preparation of that combined product produces a new product separate from each of the individual ingredients, and that may be what's causing our immune system a problem.

So it comes back to, clinically, my recommendation to people, is as much as possible, you keep going in the direction of, "Eat God-made food and not man-made foods." And you're going to be safer. We're not saying that you have to be perfect. But, if you're conscious of some of these concepts, what happens is your intuition starts to take over. And, your intuition says, "You know, I'm not sure this is so good for me to be eating this," and will cut down on the amount of exposure to some of these things.

Now the third component Dr. Vojdani referred to—it's about 8 to 10 minutes ago now, but I want to make sure that our clinicians, especially, heard this, and our moms who are trying to find out, "What's wrong with my child?"—the third component…The first one was the IgE prick test versus the blood. The second one is delayed reaction. It might not react for three, four, ten days, two weeks.

And the third was the value of multiple immunoglobulins testing at the same time, that you look at the Army, the Air Force, the Marines, all at the same time, and not just look at the Air Force. So what does that translate into? Tests that look at IgG, IgA, and IgM together. And Dr. Vojdani has been on the cutting-edge leading the charge in this concept of looking at multiple immunoglobulins—that's the IGs—multiple markers **[25:00]** of the immune system being activated so we don't miss anything.

So Dr. Vojdani, with that concept in mind, what was it that got you thinking about that, testing multiple immunoglobulins, different classes of immunoglobulins?

Dr. Vojdani: Okay. I am equally guilty, Dr. O'Bryan. In 1985, I was the one who developed food IgG testing by ELISA, which is a method of measuring IgG antibodies.

Dr. O'Bryan: Very common method today that's used today.

Dr. Vojdani: Yes. But unfortunately in many laboratories who followed my methodology, they did not involve immunologists in their laboratory and think about whatever Vojdani said in 1985, it's not correct today. And why is that? Because the way the immune system is built, any antigen or any product, any food that we eat, gets to our digestive tract, the first line of defense to become activated and make antibodies against any component of that food. When our immune system tolerance is broken, when the immune system balance is out of balance and is not working because under normal conditions we should not react to any food antigens which we consume or any proteins in the food which we consume.

But unfortunately, for some reason…If we have time maybe we'll talk about it later. But for some reason the immune system, the Air Force, and all other arms of the immune system sometimes they make mistakes. And so therefore, they react to that food and make antibodies. But the way this computer within the body is that any immune reaction which begins in the GI tract, **[27:30]** it goes through many, many steps in the body, results in IgA production, which first gets secreted in the saliva and the mucosal areas. And then the overflow of that gets into the blood.

And the main reason is that the body is trying to make antibodies against the enemy. And that IgA which the body is going to produce, it's going to sit on top of the epithelial cells, the structure of the villi. So next time if I had a reaction to gluten, next time that antibody sitting there, trying to protect my body against a reaction to gluten or to casein or to milk.

So therefore today, after reviewing the mechanism responsible for mucosal immune reaction against food which we consume, we know that IgA is the major antibody responsible. And then after that when the IgA immune reactivity is so high, plus many other factors in the gut causing the opening of the tight junction…As you know, that opening of the tight junction is the gateway to autoimmunity. So, these unwanted antigens now can get through the barrier. And then this time the blood lymphocyte will react against those food antigens, and they will make IgG or IgM. So IgA is unique to the mucosal immune response against food antigens. And IgG and IgM is more responsible for when the food antigens get into circulation, and then the body makes antibodies against them in order to control them.

But unfortunately, in all these three conditions, when antibodies in the circulation…And again, more antigens will come into contact like a lock and a key, bind to each **[30:00]**

other that activates another component of the immune system called complement cascade. And the complement binds to the antigen plus antibody to form immune complexes. And immune complexes are the most pathogenic or inflammatory molecules in the human body. And if those complexes of IgA, IgG, IgM get to the joint, [they may] cause joint abnormalities, if they get to the kidney, [they] may cause kidney abnormalities. And if they get to the thyroid, [they] will result in thyroid autoimmunities.

So that's why we have to look at all the components of the immune system. In particular, I'm talking about antibodies. We have to look at all antibody isotypes: IgE for immediate immune response, IgG, IgM, and IgA for delayed immune response. IgA specifically for the gut's immune reaction. And the IgG and IgM for other immune reactions all over the body.

Dr. O'Bryan: I'm sitting here smiling because someone sitting in a master's-level course—they've already got their bachelor's degree, and they're in a master's-level course on the immune system—this is exactly what they would be being taught right now, is what Dr. Vojdani so eloquently went through. So for our listening audience that is not sitting in a master's-level course and to try to reproduce what he just said, let me see if I can do this for you.

The mucosa is the inside lining of the tube that goes from the mouth down to the other end, the GI tract. The mucosa is the lining that really touches the outside world. Remember we've talked about when you eat food, that it's still outside the body until it's absorbed. If you had a donut and you stretched the donut out into one big long donut, the food's going down the hole in the center of the donut. And it's got to go through the walls. It has to go through the microvilli, the shags in the intestines, in order to get into the bloodstream.

So the mucosa is the lining to that inside hole of **[32:30]** the tube. The mucosa is also the lining in the lungs. Anywhere where the outside environment is connecting to the inside of the body, that's the mucosa. And the immune cells that get built first are the IgA cells. And they'll sit in the mucosa because they've already been primed from a past experience that "this food's a problem". In the example of gluten, "this food's a problem".

So now you've got IgA antibodies in the saliva, in the lining of the intestinal tract. They're just sitting there waiting so that when gluten comes through, they can grab it and they lock it up. And when they lock it up, it's a really strong bond that's supposed to be eliminated in the bowel movements. That's how our body works.

But it also can cause a little inflammation, which will cause the tight junctions—those gaps between the cells in the intestines—to open up. And now here comes that intestinal permeability, the leaky gut. And that IgA with the gluten molecule bound

together, they go through that tight junction into the bloodstream. Now this thing's in circulation. And now you can have the effects on different organs in your body, whether it's the brain or the kidney or the thyroid or the joints.

So IgA is the first one. That's why the saliva test looking for gluten antibodies is an early marker. And it's a really good marker. We'll talk in a minute about the weakness of the test is that it's only looking at one of the peptides of gluten, gliadin. And we'll talk about that. But it's the early marker if there's a problem.

Then when the IgA can no longer deal with the scope of the problem…The invaders are coming in constantly: toast for breakfast, sandwich for lunch, pasta for dinner, pancakes for breakfast, sandwich for lunch, croutons on the salad at dinner, and then a cookie. When there's so overwhelming amounts that the IgA can't be produced enough, now the IgG, now the IgM come into play.

Is that an accurate overview Dr. Vojdani?

Dr. Vojdani: Absolutely. And very, very well said, my friend!

Dr. O'Bryan: Oh, thank you, thank you! So I know this is technical for some of us listening. But this is so critical to understand.

Dr. Vojdani, with that in mind, can we now go to saliva testing? **[35:00]**

Dr. Vojdani: Yes.

Dr. O'Bryan: Okay. So the saliva testing for gluten sensitivity…You and I both were very excited in January of 2011 when that research paper came out on 5,000 Italian children that they screened with saliva testing. And they found that it was almost 100% accurate in identifying celiac disease. That was such a remarkable article because it validated the saliva testing that is now available. Can you talk about that type of testing for a moment to begin with?

Dr. Vojdani: As you know Dr. O'Bryan, in scientific journals there are—I would not say hundreds—but at least tens of articles written every year about the importance of oral fluid in medical diagnostics.

Dr. O'Bryan: Yes.

Dr. Vojdani: And as you mentioned, one of them is early detection of gluten sensitivity and celiac disease by measuring IgA plus IgM antibodies in saliva against gluten and gluten peptides.

Dr. O'Bryan: Yes.

Dr. Vojdani: And it's one of the best tests, based on my experience, which can detect gluten sensitivity and celiac disease at early stage. And so therefore, the patient can take preventative measure. Why this is so important is because we should not wait until the patient will have completely flattened tissue, meaning atrophy of the villi, and have full-blown celiac disease.

The IgA in saliva against gluten will appear, in my opinion, sometimes five years or ten years before the onset of full-blown non-celiac gluten sensitivity or even celiac disease. And therefore it's so important to do this simple test by measuring IgA plus IgM antibodies in saliva.

Dr. O'Bryan: Yes, yes, absolutely. And one of the **[37:30]** indicators for the test is someone who cannot do a blood draw or does not want to do a blood draw, saliva is easy. All you have to do is put some saliva in a tube, spit in a tube. And for children, at what age, Dr. Vojdani, is the saliva test going to be accurate?

Dr. Vojdani: That's a very good question. Based on many articles I have reviewed, it's amazing, Dr. O'Bryan, that because IgA is one of the major first lines of defense in the tube that you said starts from the mouth all the way to the bottom of the tube, IgA is produced almost three months after birth.

Dr. O'Bryan: Three months, yes.

Dr. Vojdani: Three months after birth almost we have the same level of IgA in secretions, meaning in saliva, as adults.

Dr. O'Bryan: Wow!

Dr. Vojdani: Look how beautiful nature is. As you know, when a child is born they have lots of IgG from the mother's placenta transferred from the mother to the baby.

Dr. O'Bryan: Yes.

Dr. Vojdani: And also from the breast milk, if they'll do breastfeeding, of course. But actually after birth, the body will start to rebuild its mucosal immune system. And by three months, six months, they will have the same level of IgA in saliva as you and I are having right now.

Dr. O'Bryan: Yes. That's the purpose.

Dr. Vojdani: So therefore at any age from, let's say, one year and thereafter you can measure antibodies against, not only gluten, against any other food antigen in secretion, in this case saliva.

Dr. O'Bryan: And Dr. Vojdani, are there different types of saliva tests that are out? Are there some older ones and newer ones that are more sensitive? Or are they all about the same?

Dr. Vojdani: I don't understand the question. What do you mean the old and new testing? If I understand, **[40:00]** for example, lots of laboratories are measuring IgA antibodies against various food antigens. To me, when we started doing IgG or IgA testing, we used to take crude antigens. And later on please explain to the listeners what I mean by crude. Meaning if I take wheat, I just grind the wheat and make out of that flour and then extract it, and then put it on the plate and measure antibodies against whatever is in wheat or whatever is in milk or whatever is in meat, as a whole.

But today we know if your antigens are not pure, you may not get a pure immune response or very good immune response in the laboratory settings for immune reaction or antibody detection in the laboratory setting against that antigen which you are looking for.

Dr. O'Bryan: Yes.

Dr. Vojdani: In today's technology, as you know, we have got to the level of peptides, Dr. O'Bryan. For example, alpha gliadin, you know, is 33 amino acids, like 33 beads in the necklace with different colors. If we can have a test using such a pure peptides, then the reproducibility of the test is going to be close to 100%, if it's not greater than 90%, close to 100%. But unfortunately, many laboratories are using the same old methodology, just using extract of wheat or any foods, and they put it on the plate and look for IgG, IgA, or IgM or IgE.

Unless the antigens are pure you are not going to get a good reproducible, good test. We call that a reliable test. **[42:30]** So if you mean that old tests versus new tests, that's how I'm looking at the old way of testing versus the new way of testing. The old way of testing is to use a mixture of many foods, antigens, which is mixed with thousands and thousands of unwanted factors which can cause false positives or false negatives. But when you purify an antigen, such as alpha gliadin or casein—alpha gliadin from wheat and casein from milk—and you test IgA or IgM or IgE antibodies against that, then your test is going to be extremely reproducible and sensitive.

Dr. O'Bryan: So that is a once again a brilliant explanation of why someone can get a test done by two different laboratories on the same day and get two completely different

results. It's because, what is the laboratory using as their test substance for wheat or for whatever food you're testing?

So that leads us right into the critical topic of multiple peptides of gluten. So let me begin with this question. And this is really the takeaway for our listening audience. The primary takeaway is this topic.

Dr. Vojdani, we know that 50% percent of celiac patients will have elevated antibodies to one of the peptides of wheat called alpha gliadin that you've already referred to, 50% of them. But that means 50% don't! Yet we know that celiac disease is a response to eating gluten. Yet the test that every laboratory does when they're testing for a sensitivity to gluten is looking for response to alpha gliadin.

So if the test comes back positive, likely it's an accurate test. But if the test comes back negative, we now know—and you and I have shared many studies on this, and you've educated me on this—is starting in 1999, research papers started coming out showing there are multiple peptides to gluten, not just alpha gliadin. **[45:00]** There are many different components of this poorly-digested food that can trigger an immune response.

So my question has been, "Why are we checking only one?" And there's never been a really good answer as to why, except that it just hasn't been done, until your research and your putting together these tests. We now have tests available that look at ten different peptides of gluten including alpha gliadin. But now we don't miss it if someone doesn't respond to alpha gliadin, the test from any other labs would come back negative, but they may be responding to gamma gliadin or to one of the other peptides. And we now have tests that identify that. Can you tell us about these tests?

Dr. Vojdani: Yes, thank you Dr. O'Bryan. As you know, that's one of the tests that makes me very, very, proud because there is now a meeting that I go to on monthly basis, let's say, where I meet hundreds of clinicians. And some of them come to me and thank me for developing the test, which in the past, they did misdiagnosis by measuring only antibodies against one component of wheat. And so therefore we came up with this idea…If wheat has so many components, even in the case of gluten, we have different sizes of the necklace, some of them with 18 beads, some of them with 24 beads, some of them with 33, and some of them with longer ones.

There are other peptides such as gamma gliadin, omega gliadin, glutenin, gluteomorphins, wheat germ agglutinin, this has nothing to do with germination of wheat. We are talking about 2% protein of the wheat kernel. In some individuals, **[47:30]** if they are sensitive to wheat germ agglutinin, wheat germ agglutinin can enhance overgrowth of bad bacteria in the gut causing gut inflammation and opening of the tight junctions. Or even in some cases that wheat germ agglutinin can go all the way to the joints or even to the brain, and cause abnormal immune reactions in the joints, as well as in the brain.

So the bottom line was this, that in order to get not false negative results, meaning in the other 50%, we have to measure antibodies against the major components of wheat

including alpha gliadin 30-mer whether it is non-deamidated or deamidated, then gamma gliadin, omega gliadin, glutenin, gluteomorphins and wheat germ agglutinins. By that we enhance both the sensitivity and specificity of the test, meaning those 50% who went to the doctors and the doctor told them, “You do not have non-celiac gluten sensitivity or celiac disease,” now we can help them to do that.

Dr. O’Bryan: That was a brilliant introduction for our audience of the most sophisticated test that is available currently on the market looking for a gluten-related disorder, with or without celiac disease. And I was so thrilled over three years ago when these tests finally became available. We now have thousands of doctors around the country that are using these tests.

And as in Dr. Vojdani’s experience, mine is the same way, that when we are out there teaching at different medical conferences doctors always come up to us and say, “These tests are so incredible. Finally we’re able to identify this sensitivity before the end-stage of celiac disease.” Because the blood tests for celiac disease are very, very accurate **[50:00]** if you have the shags completely worn down and it’s at the end-stage. They’re very accurate.

But they are not accurate if it’s an earlier stage. They may be positive, they may be not. And it should still tell you you’ve got a problem, but the tests don’t often do that. In fact, some studies say they can be wrong with false negatives up to seven out of ten times when the patient actually does have celiac disease, but it’s in an earlier stage.

So these tests looking at sensitivity to multiple peptides of gluten have been a godsend because not only do the patients see, “Okay, I can see that my immune system’s reacting, I’ve got a problem,” but when you clean up your diet, you eliminate those foods that your body is reacting to, and you feel better, your symptoms reduce. You can go back in six months or a year and you retest. If the immune system has come back and now says, “There’s no problem,” many people will ask their doctor, “Well, can I eat gluten now?” because we all want to eat this food that we grew up on and that is available every day of our lives. But the answer, doctors, is to say, “I don’t know. Let’s ask your immune system.” So, if you want to do an immune challenge then you go ahead and eat some gluten again.

And how much gluten, Dr. Vojdani, would a person have to eat before, and for how long, before we could expect if they had a problem and the blood test follow-up came back down to normal ranges, how long before we would recheck to see is your immune system saying, “Nope, this is not good for you?”

Dr. Vojdani: Okay. First of all, let’s explain to our listeners that the immune system is so beautiful. When for the first time our cells get exposed to a foreign material, in this case gluten, it will react to it and eventually will make antibodies, IgA, or IgG or other antibodies against that. So the antibodies are going to be detected in blood or in saliva

for probably a month or two or three months, but after that they will go down. **[52:30]** But this is only if really we are exposed for the first time in our life and certain amounts of wheat or gliadin got in contact or our cells got in contact with it.

So when the antibodies are gone, our lymphocytes, our white blood cells, are going to have a computer within called memory cells. [They] will have hundreds or thousands or millions of cells in our blood and in our tissue, which remember that a few months ago or few years ago they had exposure to gluten.

So the second time we get exposed, those memory lymphocytes immediately go into action and react to the wheat, and immediately. This time they're not going to wait for two weeks or three weeks to make antibodies. It will take only few days to make that antibody and immediately try to fight against the foreign invader.

But Dr. O'Bryan asked the question, "How much antigen do we need?" There is a huge difference when for the first time we get exposed to an antigen and our lymphocytes react to it and make antibodies, the amount of antigen—in this case gluten—needed will be about the size of a kernel of the wheat, a few milligrams.

But when we have the memory cells for the second time or the third time or the fourth time, when we react, we need one hundred or one thousandth of that few micrograms of glutenins in us to go to the computer in our white blood cells and say, "Wake up! The foreign invader is here. React to it and try to get rid of it." So we are talking about milligrams, which is about the size of a kernel of the wheat, not a bite of sandwich from a sandwich. We are talking **[55:00]** about small quantities. And then the second time or the third time will be much smaller than that. It's hard even to explain to you how much that will be. Sometimes even, you are not going to see that with the naked eye.

Dr. O'Bryan: This is so critically important! And please tell me if this visual is correct. This is the mechanism by which our vaccinations work. We receive maybe a milligram of a measles bug in a shot. And then our immune says, "This is a problem," and builds the mechanisms to produce the antibodies—I call it the assembly line—making the antibodies. And those antibodies are soldiers trained to go after measles. And they go all through the bloodstream going after measles.

When all of those measles bugs have been destroyed from the initial vaccination we don't make those antibodies anymore. But now we have a memory B cell whose job is to be vigilant for the rest of our lives. They're in the lymphocytes, so they're circulating everywhere. So if any measles comes back into your bloodstream, if you're ever exposed, we just have to flip the switch and then you start making the antibodies, which is why if you're going to Africa, you need vaccinations months and months ahead of time for these strange diseases that are there. But if you go back to visit ten years later, you just need a booster shot two weeks before you go. You just have to wake the

system up again. So we have this system inside our body that is always vigilant to protect us against measles.

And Dr. Vojdani, is it correct to say that's it's the same mechanism when we develop elevated antibodies to foods, that that same mechanism to protect us, those memory B cells, are now in the lymphocytes and they're with us forever?

Dr. Vojdani: Yes, Dr. O'Bryan. We have only one mechanism in this case, memory immune reaction. For the first time it's called, "primary immune response." The second time it's called, "secondary immune response." And, tertiary, and the fourth, and the fifth, it's all based on memory lymphocytes reacting to the antigen.

Dr. O'Bryan: That is why if we order a salad in a restaurant, and they bring us croutons **[57:30]** by mistake, you can't pull the croutons off. You have to get a completely new salad because a couple of crumbs from the croutons that you cannot see—remember, 1/1,000th, the initial dosage for the vaccination—is all it takes to activate the memory cell and start that whole inflammatory mechanism producing the antibodies.

So Dr. Vojdani, with that concept in mind, here's a question that I've wanted to ask you. And I've just not thought to ask you when we've been together in the past. With that concept in mind, that those memory immune cells are now in circulation to protect us, how is it that in the past there has been this concept of rotation diets? That it's okay to have a food you're allergic to once in a while, as long as you don't get any symptoms from it?

My thought has been it's not okay because you're going to produce the antibodies causing the permeability. And then the mechanisms that might occur somewhere else in your body, that you can't feel when your brain cells have antibodies that are slowly destroying your brain tissue. So if you have any exposure to a food that you've had elevated antibodies to, that really suggests that it may need to be a permanent elimination of that food.

What do you think about that concept?

Dr. Vojdani: Dr. O'Bryan, based on that question I see you became a very good immunologist, and I appreciate that. As I said earlier, I equally am guilty of the past thinking. And many people thought that way, even so many laboratories. These days they do food sensitivity. And they give them rotation diets. And sometimes I have seen a laboratory giving them like a Visa card. And the foods which they react against are written on a card which is in their pocket, it's very beautiful, it looks nice. But from an immunological point of view, it doesn't make sense.

If you are reacting to one food or ten different food antigens, you have to remove them from **[1:00:00]** your diet forever. That's my opinion. There will be zero tolerance. If you

introduce them after a few months or a year, this time your immune system is going to react violently to them, and will make a hundred times more antibodies. And therefore autoimmune reactivity could be much stronger than before.

Dr. O'Bryan: Thank you for that. That's a point that comes up every once in a while when someone has eliminated gluten and dairy from their diets after seeing on a test that it's a problem. Somewhere down the road they have an inadvertent exposure, and they seem to feel so much worse than they used to feel when they were eating it. They had headaches, they went on a gluten-free diet, the headaches went away. But then they have an exposure to gluten five months later, and the headache is one of the worst they've ever had. It's a worse reaction.

Why is that? What's the mechanism behind the severity of reactions that some people notice when they have an exposure after eliminating the food?

Dr. Vojdani: Yes, thank you. Again, exactly, based on memory lymphocytes. They are on a gluten-free diet then their memory lymphocytes are quiet. They're sitting in the tissue, no reaction, no antibody production. As soon as they go back on eating gluten or other food antigens, their lymphocytes will react to this and will make hundreds, tenfolds more antibodies than they had before. And this time those antibodies will go to different tissues.

If it's in the brain, they will cause a severe headache and other abnormalities as well, because you used headache as an example. And so again, it's based on the memory lymphocytes which are going to react to the new food antigens consumed by the patient, and, therefore severe immune reaction equals the induction of severe symptomatology.

Dr. O'Bryan: So our listening audience has heard in many other interviews in this summit, Dr. Loren Cordain talking about wheat germ agglutinins, **[1:02:30]** and Dr. Fasano talking about gluten causing permeability and the complications can be autoimmune diseases, and Dr. Yehuda Shoenfeld talking about how identifying those antibodies can be of such value.

Our audience has heard that the complications of gluten are not just the symptoms they feel that get better on a gluten-free diet, but the underlying aggressive inflammatory cascades that develop attacking tissue, the autoimmune processes that are determined by your genetic vulnerability and the antecedents, how you've lived your life. Do you have a lot of mercury or a lot of aluminum or things like that? So our audience has heard that.

So the answer to the question…I'd like to see if you agree with this, Dr. Vojdani. My clinical answer for our patients has been, "Well, can I eat gluten now that my antibodies

are down?" The answer is, "Probably not. But rather than it be my idea and then you're going to fight me on it, let's just ask your immune system."

Dr. Vojdani: That's a very polite way to say no.

Dr. O'Bryan: Yes it is, because they'll go back and they'll eat the food for a while, and then a month later we'll do the blood test again. All of a sudden the antibodies are back higher than they were before.

Dr. Vojdani: Dr. O'Bryan, to ask the immune system, and when the immune system will react to that, sometimes will be too late because that immune reaction now going to attack their joints. It's going to attack their thyroid or their cerebellum in the brain.

Dr. O'Bryan: Yes.

Dr. Vojdani: And therefore we have to very careful.

Dr. O'Bryan: Exactly right! We have a handout that's available to all of our summit attendees on the gluten challenge and why it's not recommended. So, I want to be very clear, we don't recommend the gluten challenge because it can cause lots of complications as Dr. Vojdani is saying, a hundred, a thousand times stronger reaction by the immune system producing these antibodies.

But the danger is these mechanisms that you don't feel when you do a gluten challenge or if you have it once in a while on a rotation diet. You don't feel the headaches you used to have sometimes. But the autoimmune mechanisms continue, and continue attacking your brain or attacking your heart or attacking your kidneys or attacking your joints. **[1:05:00]** And as it continues to attack and attack and attack, we all know—and our listeners have heard me say this before—"No one gets Alzheimer's in their sixties and seventies. It happens in your twenties and thirties, and it just takes 30 years of killing off brain cells before you start noticing the symptoms." These autoimmune conditions are decades long.

So the idea of a rotation diet…If you check your immune system and your immune system is not reacting, then we have no scientific argument that I can think of as to why you can't eat that food. But if you check and your immune system starts elevating the antibodies again, then you know. But let me check that with you, Dr. Vojdani.

If they are identified as gluten sensitive, they go on a gluten-free diet, rechecking in six months or a year all the elevated antibodies have come down to normal. That's all of them, not just some of them, but all of them have come down to normal. And they want to do a gluten challenge—I don't recommend it, but they want to—so, we tell them how to do it properly. And they do the gluten challenge. A month later they do the test, and it

comes back there's no elevated antibodies to gluten. Is it all right for them in that situation to continue eating gluten?

Dr. Vojdani: Some doctors may say yes. My opinion is no because if they have gluten again, the memory lymphocytes will react this time, will have more antibodies produced, and those antibodies will attack their tissue. Years later, they may develop full-blown autoimmune disease.

Dr. O'Bryan: Yes. And, that is the answer that I would have thought of also. So you check the gluten antibodies are negative, but you also have checked the autoimmune antibodies to see if they have become elevated.

So let's take just a couple more moments if we can, Dr. Vojdani, and talk about how do we identify if there is an autoimmune mechanism going on in our bodies that we don't yet have symptoms from?

Dr. Vojdani: As you know, there are many laboratory tests for measuring autoimmune disease. First I'm starting with disease.

Dr. O'Bryan: Yes. **[1:07:30]**

Dr. Vojdani: And in my laboratory we do tests for antinuclear antibodies, called ANA. We do tests for rheumatoid factor. As you know, it's associated with rheumatoid arthritis. We do measure anti-DNA antibodies, which is associated with lupus. We measure total immune complexes, which is associated with general inflammation. But these tests, which I do perform in my laboratory, are not going to be positive unless the patient is having full-blown autoimmune disease, lupus for example. But as you know, you and I are not interested in detection of the disease because when the patient is having full-blown lupus or arthritis, the only choice we have is to put them on immune suppressants for the rest of their life.

You and I ask the question, "Why [does] the body react to its own tissue?" The body under normal conditions should not react to its own tissue antigens unless either some foreign material, such as Epstein Barr virus, cytomegalovirus, herpes type 6, or gluten, or casein manage to get to our blood where our lymphocytes will react to that, will make antibodies against Epstein Barr virus or casein or gluten.

But unfortunately, because of the similarity between the structure of the virus or gluten with human tissue, now our own soldiers are going to attack our own tissue, **[1:10:00]** which can result first in autoimmune reactivity. And if we do not detect autoimmune activity at an early stage, ten years later we will have full-blown autoimmune disease.

So my point here is that we have to detect the triggers which are responsible for induction of autoimmune reactivity and not wait until the patient will have full-blown

autoimmune disease, which will put them for the rest of their life on an immune suppressant or an anti-cytokine, such as anti-TNF alpha, in a case of rheumatoid arthritis.

So we are interested in early detection. So the result if we do testing and the patient is making antibodies against gluten, or the patient is making antibodies against heavy metals, by removing the heavy metals or Epstein Barr virus or gluten from the environment of the patient now the triggers are not going to activate our lymphocytes to make antibodies against the trigger, as well as our own tissue. Therefore the autoimmune reactivity slowly will go away. And in this case we are going to prevent induction of full-blown autoimmune disease.

So there is a huge difference between autoimmune reactivity versus autoimmune disease. In the case of the autoimmune disease, we cannot do so much for the patient, only by treating the symptoms of the patient. But in the case of autoimmune reactivity, if we detect the trigger and we remove the trigger, and we repair the barriers, we are going to make a huge difference in the life of those individuals with the possibility of developing autoimmune disease in the future.

Dr. O'Bryan: That is a brilliant overview that clearly gives the vision as to why it's so important to identify these triggers. **[1:12:30]** There are many, many cases in the medical literature of reversing the autoimmune reactive antibodies, reversing, actually, some of the autoimmune diseases that are beginning when you get the environmental triggers out of there.

And in this summit we're talking mainly about gluten. And of course casein from dairy comes up quite often with that. But there are a number of them. But this is the mechanism and the reason why you want to identify, what is your immune system fighting? Because those products that your immune system are fighting, whether it's gluten or dairy or mercury, those products, they have a similarity in their molecular structure to some of the tissues in our body. And we begin making antibodies to gluten, and then we begin making antibodies to the tissue, like a thyroid, because it looks like gluten.

Some of the amino acid structures are very similar, or in some cases identical. And so you start slowly killing off your thyroid cells, slowly killing them off. And when we get the gluten out of there, many times—and there are a number of papers on this—you see the antibodies to the thyroid going down and back to normal ranges when you eliminate the environmental trigger, gluten in this case, from their diet.

This is the cutting edge work that I have been trained by Dr. Vojdani on over many years now that I'm hoping our entire listening audience will understand, and why you'll want to listen to this interview again and again and again to become familiar with these overview concepts. If there's one thing you walk away from in this summit, A Grain of

Truth, it is that the environmental triggers we're taking in—in this topic it's gluten, it's one of the most common ones—contribute to the development of the autoimmune reactive syndromes that eventually go to autoimmune disease, which is the number three killer in the world today, is autoimmune diseases. And if you can identify this and get it out of there, you'll reduce your risk of developing these autoimmune syndromes.

Dr. Vojdani: I would like to give you another example, Dr. O'Bryan. It is very well accepted in patients with full-blown autoimmune disease, such as **[1:15:00]** lupus, who makes antibodies against DNA, they do plasmapheresis. Plasmapheresis is the process by which we filter the antibody in the blood of the patient. The blood goes through a filter, the antibodies stays in the filter, and the blood goes back to the patient's circulation.

Dr. O'Bryan: Yes.

Dr. Vojdani: There are many articles in scientific journals showing that during plasmapheresis, patients' symptomatology goes away for at least four or five weeks.

Dr. O'Bryan: What? What?!

Dr. Vojdani: Yes, what did we do in this case? We removed the antibodies. So by eliminating the environmental triggers at an early stage, what are we doing? We are removing the production of antibodies against the triggers which are responsible for attacking our tissues.

So which one is better? To wait until the patient will have full-blown autoimmune disease and do a plasmapheresis, removing the antibodies? Which is not bad. But the best way to approach this is to detect antibodies at an early stage. So by removing the triggers, you are going to eliminate the antibodies in patients' blood. And the patient will be healthy forever, hopefully.

Dr. O'Bryan: Well, that's a beautiful vision to conclude on. And Dr. Vojdani, I want to thank you so much for taking the time to share this with us today. And hopefully tens and hundreds and thousands will be moved forward in their understanding of the underlying mechanisms that eventually may contribute to their illnesses and their getting sick and shorten their life span as a result of this particular interview today.

Thank you so much for joining us!

Dr. Vojdani: And, Dr. O'Bryan, I was honored to be interviewed by you, in particular. Any immunological terminology I used, you made it much, much simpler to our audience to understand those immunological terminologies. And I appreciate your input.

Dr. O'Bryan: Thank you very much!

Dr. Vojdani: Thank you!

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