A Grain of Truth: The Gluten Summit
Presenter: Dr. Loren Cordain, PhD

Wheat Germ Agglutinin: How a "Monster Molecule" Could Affect Every Cell in Your Body

Dr. O'Bryan: Hello, everyone! Welcome to another edition of A Grain of Truth: The Gluten eSummit.

I am thrilled and honored to be here today with Dr. Loren Cordain, the godfather of the Paleo Diet. Dr. Cordain is a professor in the Department of Health and Exercise Science at Colorado State University in Fort Collins, Colorado.

He is widely recognized to be one of the world's leading experts on the benefits of the natural diet of our Stone Age ancestors for contemporary people. Dr. Cordain's scientific publications have focused on the nutritional characteristics of the wild plant and animal foods consumed by foraging humans across the globe, and the ways in which such a diet can benefit the health of modern humans.

He is the author of more than 100 peer-reviewed scientific articles and abstracts, many of which were funded by both private and governmental agencies. And, he has lectured internationally on the concept of Paleolithic nutrition.

His research into the health benefits of Stone Age diets for contemporary people has appeared in the world's top scientific journals, including *The American Journal of Clinical Nutrition*, *The British Journal of Nutrition*, and *The European Journal of Clinical Nutrition*.

Dr. Cordain was the recipient of the Scholarly Excellence Award at Colorado State University for his contributions into the understanding of optimal human nutrition. He is the author of *The Paleo Diet*, *The Paleo Diet for Athletes, The Dietary Cure for Acne, The Paleo Diet Cookbook,* and *The Paleo Answer.*

Dr. Cordain, thank you so much for joining us today at A Grain of Truth: The Gluten eSummit!

Dr. Cordain: Tom, it's my pleasure. I'm happy to be here with you.

Dr. O'Bryan: Thank you. Can we begin with what got you interested in this topic of gluten and its potential impact on the human system?

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Dr. Cordain: It's partially personal that dates back to 40 years ago, kind of realizing that I may have had some health symptoms that were associated with eating gluten. When I was a young man in my twenties, I recognized that. But, moreover, it has to do with the concept that our research group has developed. And, that is this concept of evolutionary medicine commonly known as the Paleo Diet. **[2:30]**

And, so, it was brought to my attention by a very now-famous paper by Boyd Eaton in *The New England Journal of Medicine* in 1985 that humans, before agricultural times, basically, did not consume cereal grains. And, so, that notion kind of clicked. And, I started researching that 25 years ago, started compiling articles, and started to see that the cereal grains, particularly wheat and gluten-containing grains, have a number of toxic components that affect many people beyond celiac disease.

Dr. O'Bryan: And, when you say, "toxic components," for our listening audience, what do you mean by that?

Dr. Cordain: Well, I think for the average person, when they hear the word toxic it sounds like poisonous, lethal, whatever. But, actually, people that study toxicity...Toxicity can range from very subtle effects, as I mentioned, to lethal effects that are somewhat dose-dependent, meaning that the more you get, the more it seems to adversely affect our physiology. So, when we talk about cereal grains, particularly gluten-containing grains, they have a variety of elements or compounds that are toxic, not just to us, but to other mammals, to birds, and to insects.

And, indeed, that's why cereal grains have evolved these--what are called secondary compounds or antinutrients--is to protect them from predation. So, when you think about a cereal grain, it is a seed. And, that is the reproductive material of a plant. And, if the reproductive material of a plant cannot get into the earth and reproduce, then that plant becomes extinct very, very, rapidly.

So, plants have taken a number of evolutionary strategies to prevent predation by birds and insects and even pathogens, fungus, and bacteria and so forth. And, there are essentially three strategies that plants have taken to overcome predation by these animals or organisms. **[5:00]** And, one is that they evolve structures like thorns and hard shells and physical barriers to the seed so that it's very difficult for the predator to get to the seed so that the seed can get into the ground and reproduce.

They also have evolved another evolutionary strategy, which is really quite clever. They've evolved fruit so that predators actually want to eat their seeds. The seeds are very hard and impervious to digestive juices. So, for instance, when you eat a strawberry, it's got tiny little seeds on it on the outside. And, those seeds pass through the GI tract and get into the feces and are now taken to a new spot and loaded with fertilizer. So, that's another strategy.

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But, cereal grains and legumes have taken on a strategy in which they have evolved toxic compounds, compounds that do a couple of things. They increase intestinal permeability so that the toxic compound can get past the GI tract barrier and into the bloodstream. So, you have to have those two components available to cause the toxic effect. So, in other words, if poison can't get into our system, then it can't do its damage. And, so that's nutritional characteristics that legumes and cereal grains have is they both have compounds that increase intestinal permeability. And, then, they have a variety of compounds that interact with our physiology to produce effects.

Dr. O'Bryan: These toxic compounds in the seeds, are they more concentrated in the finished product that humans eat in terms of flour-produced products or flour-containing products? Is there a higher concentration of these toxins which would impact on the human digestive system causing permeability?

Dr. Cordain: Well, actually the way we eat most of our cereal grains...When you talk about flours, you can make flours out of nuts. And, you can even make flours out of legumes and many plant products, including potatoes and whatever. **[7:30]** So, "flour" is kind of a nebulous term. I would prefer to talk about cereal flour, which is what most of us consume. And, the primary cereal flour that we eat is wheat, followed by corn flour and sometimes rice flour.

But, the way we eat wheat flour is we eat it refined, meaning that the endosperm or the white part of the seed of the wheat is what remains. And, we basically throw out the bran and the germ. So, from our laboratory and others around the world, what we've done is we've analyzed the concentrations of these antinutrients. They tend to be highest in the bran and the germ, and lowest in the endosperm. So, surprisingly, we actually get--and it depends on which toxic compound you're looking at--but, surprisingly, we get lower concentrations of all antinutrients when we eat refined flours.

Dr. O'Bryan: That is surprising. And, is the toxic level, even in the refined product, enough to contribute to the development of intestinal permeability in humans?

Dr. Cordain: It depends on which one you're talking about, for instance, wheat. There are three compounds in wheat which we know cause intestinal permeability. The best studied of which is gluten, or, actually, a protein called gliadin. And, so, there's many gliadin proteins. But, they all seem to increase intestinal permeability. The mechanisms by which this works have been elucidated by Alessio Fasano's group at the University of Maryland, starting in a series of papers from about 2006 onward. So, we now have a real good idea of how gliadin or gluten increases intestinal permeability. It seems to be variable in its effect. Some people, it doesn't seem to affect as much as others. So, that information, we're still working on it.

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There are other compounds in wheat that increase intestinal permeability. And, the one that our group has studied directly is wheat germ agglutinin or WGA, which is known as a lectin. And, WGA **[10:00]** seems to increase intestinal permeability through two pathways: paracellular and transcellular pathways. And, we're not sure if both or one or the other is operative in humans. But, at least from animal models and tissue culture models, it seems that both probably are working. In other words, the WGA or the lectin can go between cells or it can go through cells through receptor-mediated pathways.

The third component in wheat that increases intestinal permeability is an obscure protein called thaumatin-like proteins. And, this has been studied in other plant products, but not so much so in wheat. So, we suspect that wheat actually has three compounds: gliadin, WGA, and thaumatin-like proteins that seem to act synergistically to increase intestinal permeability in some people to some degrees, and in some people perhaps less.

Dr. O'Bryan: Well, that's fabulous information. And, that's a new concept for me about the third component of wheat, the thaumatin-like proteins. Has that been elucidated in the literature in humans, that the thaumatin-like proteins can be an antigen?

Dr. Cordain: Well, whether or not it's an antigen is unclear simply because we haven't done those experiments yet. So, the information is triangulated from animal studies, from tissue studies. But, in terms of direct human studies--in other words, feeding people wheat and seeing if thaumatin antibodies appear in sera--have not been done. And, the reason that I say such is that the entire world--it's kind of like cigarette smoking in the fifties--the entire world eats wheat. And, so, we don't think upon wheat as being a toxic compound per se because everybody seems to do it and seems to get by okay with it.

But, I think there are subtle effects **[12:30]** that influence our immune systems, inflammation that affects cardiovascular disease, cancers, and other diseases that are not very well appreciated. So, thaumatin-like proteins, no. And, the point I wanted to make is wheat germ agglutinin, WGA, has been hugely studied in literature. If you go to Medline and you type in "wheat germ agglutinin" or "WGA," you'd be inundated with tens of thousands, perhaps hundreds of thousands of articles because it is used as a compound by molecular biologists to isolate cellular effects. And, the reason that it does so is because WGA binds everything. It binds everything. It's like superglue. If it gets into the system, it screws up everything.

And, so, that was our real interest, was to see if WGA that people consumed actually gets into the bloodstream and gets to tissue. So, that's what we bring to the table with kind of our information internationally. And, you would think that a compound that it has such potentially toxic effects would have been studied. If the USDA were to approve

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WGA as a generally-recognized non-toxic substance, it would have to go through incredible trials.

Well, we eat this stuff on a daily basis, and what our group has done is to look to see if when you eat concentrated sources of WGA, whole wheat or wheat germ, does this stuff get into plasma? So, a couple of my graduate students that I've been working with for the last four or five years, we've done those human experiments. We've worked with a group from Austria, as well as a group from Italy. And, we developed a test called an ELISA in which we can measure WGA in human plasma. So, we carried those experiments out.

Dr. O'Bryan: What did you find in those people that you tested to see if they had WGA in their bloodstream? Is it that there's a percentage of people who will have it? Or, is it a high percentage? A mid-level? **[15:00]**

Dr. Cordain: The experiment that we ran was the first one ever done on humans, believe it or not. And, we published it in *FASEB--Federation of American Societies for Experimental Biology*--at their annual convention in 2011 as an abstract. So, we haven't published the full work because we were in completely unchartered waters.

It's like Columbus sailing to what he thought was Japan or China or Asia. He didn't realized that North America lied in between. So, he had no idea where he was when he landed in the Caribbean. And, in the same way, we had no idea what was going on with WGA in the bloodstream after people ingested WGA. So, that was really the challenge. And, we didn't get it right. So, we now realize the mistake we'd made. But, it was the first experiment we had done.

So, let me just explain to you how that experiment went and where we think we went wrong. So, we know from earlier work from Arpad Pusztai's group at the Rowett Institute in Scotland, he and his group had been working on this problem for, perhaps, 20 years or more. And, they had done animal experiments in rats and in mice. And, they had found that you feed rats and mice wheat germ agglutinin, concentrated sources of wheat, it ends up in the plasma. So, we thought it was going to be a shoo-in to find this in humans.

But, what we ended up doing was we fed college students--healthy young college students, about fifteen of them--we fed them about a quarter pound, which is a lot, about 100 grams of wheat germ. So, you go can down to the health food store and you buy wheat germ. That's basically what we fed them. And, then we put in, what are called indwelling catheters into their bloodstream. And, we monitored the concentration **[17:30]** of WGA in their blood using this test that the Austrians had developed. We actually shipped the blood to Austria to do the measurement.

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And, low and behold, we found nothing!

Dr. O'Bryan: That's startling!

Dr. Cordain: [Laughs]. Actually, it's not. So, like I said its like not realizing that North America lays between Europe and Japan. So, the problem is that we believed that WGA through gluten, through thaumatin-like proteins, and through its own interaction on intestinal epithelia, actually did get through. So, we believe that it did get through. But...And, I'm not sure what group I'm speaking to, if this is a medical group or just?...

Dr. O'Bryan: Both. It will be both.

Dr. Cordain: Yeah. So, basically, when you draw venous blood, when you do a blood draw, what you're pulling out is whole blood. Okay? So, you're pulling out whole venous blood. And, then what you do is when you measure things in blood, we typically put the blood into a centrifuge, and we spin it down. And, when we spin it down, what happens is that the red blood cells and the white blood cells and platelets and all the formed elements, they all get to the bottom of the test tube in the centrifuge. And, what remains is called plasma.

And, so, that's what we did with our samples. We spun the blood down. We measured plasma. And, guess what? We threw out the baby with the bath water. We threw out all the formed elements. So, what we were relying on was the plasma proteins. And, there's about 60 major plasma proteins, the most concentrated of which is called albumin. And, then, what we were relying on was the WGA would bind plasma proteins, and we would find it in plasma.

Guess what? Of the 60 plasma proteins--albumin, all the major plasma proteins--don't bind WGA. We know that from tissue studies. There's only one plasma protein **[20:00]** at less than 1/100th of a percent of all the plasma proteins that binds WGA. So, if it did bind that, we would have never found it. So, it's kind of like looking for a penny on a mile wide beach, you're just not going to ever get it.

Dr. O'Bryan: Now, does that point that our binding capacity for WGA is so minuscule, is that a further point to the argument that this is not a food meant for humans?

Dr. Cordain: No, exactly the opposite. What it means is that it's bound...When you bleed, the major elements are red blood cells and white blood cells. That's the primary volume-by-mass measurement are your cells that are in your blood. So, what had happened is that we believe that WGA got into the lymph. And, after it got into the lymph, it got into the blood. And, it immediately was binding cellular receptors or cells. So, was binding erythrocytes. It was binding white blood cells. It was binding platelets. Platelets are the formed elements in blood that cause blood to clot.

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So, that's what we believe had happened is that it primarily binds all of these cells in the body. And, that's how it's transported throughout the body and it gets into, we believe, every cell in the body in hours of ingestion of wheat. So, we ran the wrong experiment. [We] should have not thrown the cells out of the whole blood and measured plasma. We should have measured the formed elements. So, we think that's exactly what had happened with wheat germ agglutinin.

Now, why does that matter? So what? What if WGA does get into the cells after you eat wheat? This is an unappreciated effect of wheat. And, I know that you are very much interested in celiac disease and other effects, as the world is, of gluten on behavior and whatever.

One of the novel things we bring to the plate in a couple of papers we published is that wheat-eating impairs vitamin D metabolism. **[22:30]** And, when I first got onto this, we had looked at the animal studies. You can go back to the classic studies in which they were trying to create rickets in animal models way back in the 1980s. The way they did it was they fed puppies whole grains. They fed them wheat. They fed them whole corn, all kinds of whole grains. And, when they got to about 45 to 50% of total energy from grains, they could induce rickets.

And, so at the time, in the 1920s, the notion of vitamins hadn't been developed yet. And, so, vitamin D simply had not been discovered by that time. So, finally, they realized that feeding animals lots and lots of grains causes rickets, which is a bone disease that causes pelvic deformation in women and increases death during childbirth. It causes bowing of legs and all kinds of problems associated with bone mineral metabolism.

So, at the time in the 1920s, they had no idea what eating high amounts of grains or wheat, how and why it worked. And, so, in the 40s and 50s after vitamin D had been discovered, this research is kind of put aside. And, the idea that grain eating caused rickets was just assigned to the low level of calcium in grains and high level of phosphorus. So, the calcium-to-phosphorus imbalance seemed to have been thought to cause rickets. Well, we thought otherwise.

And, I think what's going on is that WGA gets into plasma. Wheat germ agglutinin binds what's called the nuclear pore in cells. And, so, all cells contain a nucleus. And, the way in which signals from the cell or outside the cell cause transcription of genes in the cells can occur two ways. They can occur through receptor-mediated mechanisms directly at the nucleus. Or, those signals can move what's called the nuclear pore. And, it's a small little hole in the nucleus. What happens is that **[25:00]** the WGA, wheat germ agglutinin, it actually binds the nuclear pore. And, it prevents any substance that uses a nuclear pore for causing gene transcription working.

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So, vitamin D, we all know, is associated with health, bone mineral health, prevention of cancers, even heart disease. In order for vitamin D, which plays a role in it all--it's a hormone--in order for it to work...It's a very small molecule. And, so, it actually goes through the nuclear pore. And, the problem with WGA is WGA blocks the nuclear pore. It sits on it like a 2x4 and prevents anything from going through. So, that's kind of a working hypothesis for the reason that cereal grains--and wheat, in particular, gluten-containing grains--cause so much damage, is that the WGA gets into the cells of virtually every cell in the body and it binds the nuclear pore.

So, this is kind of a concentration graded-driven phenomenon, meaning that the more you eat, the more it happens. And, then, WGA has a half-life in cells of about four hours. So, it blocks it up. Well, that's about the time we eat again. You eat breakfast and lunch. And, if you eat wheat at every meal, then you're binding the nuclear pore. So, it seems to adversely affect vitamin D metabolism through that mechanism as well as the others.

Dr. O'Bryan: We know that WGA can pass through the blood-brain barrier. That's the shielding that's protecting the brain. So, these larger molecules can get into the brain. And, the nervous system in the brain called the glial cells can be activated to fight this molecule that's getting in, causing more inflammation. This may be one of the mechanisms contributing to some of the brain conditions that we see associated with wheat sensitivities.

Dr. Cordain: You know, you're absolutely right, Tom. And, it's now well recognized that people with neurological complications--not just celiac folks, but people with cerebellar ataxias, dementia, any sort of degenerative central nervous system, particularly peripheral, and neuropathies, **[27:30]** axonal or demyelinating types, or even myopathies--seem to respond well to gluten-free diets. So, this is a strategy that many practitioners are taking, is to work with people with these ataxias, and get them off of a gluten-containing diet.

And, whether or not its WGA or other components of wheat that are interacting with the nervous system to cause ataxias are not completely clear at this time. So, there's a world of research that needs to be done with what's wrong with wheat. "Gluten" has become a buzz word. "Gluten-free diet" is the buzz word of the 21st century. Everybody's doing a gluten-free diet. Yet, only 1%, which is actually quite a bit--three million people or more of the U.S. population--have celiac disease. But, Fasano's group estimates that 5% to 7% are gluten sensitive for a variety of reasons, one of which may be ataxias.

Dr. O'Bryan: Yes. That's five to seven times higher than what we know is the ratios for celiac disease. And, condition-specific papers have been coming out that show--for example, with irritable bowel syndrome, with IBS, which is the most common presenting complaint in gastroenterologist's office is IBS--about one percent of those people are

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celiacs. But, about 30% of those with IBS have gluten sensitivity, non-celiac gluten sensitivity. And, when you take gluten...

Dr. Cordain: Yeah, that's wonderful. That's amazing news! And, you can extend it, too, to autoimmune disease. And, our group--13 or 14 years as a group--we've written papers that are way ahead of the envelope. If you can go back to 1999, you can see what I've written in a paper called "Cereal Grains: Humanity's Double-Edged Sword." We were saying this almost 15 years before it was being recognized in the clinical literature, and even from the theoretical prospective.

So, we're now, as I'm in the swan song of my career, I'm getting ready to retire at CSU. What we have been working on primarily is how gluten-containing grains--wheat, and other components not part of the original Paleo Diet, **[30:00]** dairy and so forth, and legumes--how all of these seem to be involved as an environmental trigger with autoimmune disease.

So, one thing I've never really mentioned on any interviews, and I'll grace your program with this and tell you what we think is going on is that we think that WGA is kind of like a...What do you want to call it? A monster molecule. WGA just doesn't bind human cells. WGA binds all types of cells. And, so our biome--the bacteria and the viruses, the flora of our gut--contain cells as well. So, when you eat wheat it binds those cells as well as binding our epithelial cells.

And, what happens is that we have what are called proteases or enzymes in our gut that break up these bacterial cell walls. And, bacterial cell walls are composed of proteins. And, they're also composed of the compound called lipopolysaccharide or LPS. So, what we think is going on is that WGA serves as a monster molecule. And, it's kind of like a chemist in your gut. What it does is it binds these busted up antigens or proteins from bacteria. And, it binds LPS. And, then it gets through guts. So, you've got this kind of triad of molecular compounds that are moving through the gut.

Normally, we have cells in our gut called dendritic cells that sample what's going on in the gut. But, it turns out that there is a receptor-mediated mechanism in dendritic cells that binds up WGA, binds up LPS. So, the LPS, WGA, and the antigen from the bacterial cell wall all are brought through and processed by dendritic cells. And, so, many immunologists, and ourselves included, believe that the dendritic cells then present these **[32:30]** chimeric or monster molecules to circulating T cells.

And, we believe that in genetically-susceptible people--people with HLA haplotypes--this is an absolute disaster. And, we think that this is the reason...You'd mentioned clinically that irritable bowel, ulcerative colitis, Crohn's, and so forth, many of these people do quite well when they go on paleo-type diets. And, we think that getting the grains out is

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one of the major things, particularly gluten-containing grains, because of what WGA has the potential for doing in terms of setting off the immune system.

Dr. O'Bryan: That's incredible information. So, you've got this super molecule, this monster molecule, that gets absorbed into the bloodstream. And, its almost--if the WGA is wrapping around the LPS--it's almost like a force field that's protecting it so that the LPS becomes so much more toxic now in the body.

Dr. Cordain: And, remember the results of the experiment that I told you is that we measured WGA and plasma, and came up empty handed. Well, that's not surprising. It's not surprising at all because dendritic cells are the cells in the gut, as well as other white blood cells, they're the ones that initially handle the insults of antigens that break or bypass the gut barrier.

And, one other final point here is many--since you have somewhat of a sophisticated audience--is that all epithelial cells contain on their outer surface what's called a glycocalyx. So, let me give you a quick example. When you look at a cross-section of an artery...So, take an artery. And, cut it in cross-sections so you're looking at a circle. Even most cardiologists don't realize that red blood cells and white blood cells that flow through the artery, they never touch the endothelial cells. They never touch it because there's a barrier. And, that barrier, in all epithelial cells is called the glycocalyx.

And, it's this formation of kind of feathery carbohydrate-like structures that...**[35:00]** Think about it as like when you're taking a shower, it's kind of like the hair on your head is that it flattens out against your head. And, then you get out of the shower and you fluff your hair up, and it goes up. So, that's kind of how the glycocalyx works in epithelial cells is it prevents the actual touching of one factor to another at the edge of an epithelial cell.

So, the gut is the same way. The gut has an epithelial cell. So, all the epithelial cells in our gut, when we eat food and protein and fat and everything else, is we don't absorb macromolecules right. And, one of the reasons we don't is because glycocalyx serves as a sieve to prevent any protein or amino acid from getting through because it literally is a sieve. It prevents large molecules from even getting to where they need to be absorbed. So, we only absorb intact fatty acids and sugars and amino acids.

So, guess what WGA does? WGA and all lectins...And, many--not all, but many--lectins, particularly legume lectins, bind the glycocalyx. And, they cause it to shed. And, when the glycocalyx is shed, then it exposes the bare epithelial cells to whatever the contents of the gut are, or the bloodstream, or whatever. And, so, not only does WGA serve as a monster molecule once it gets into the system, it also has molecular capacity to break down the protective component of the system. The glycocalyx is like the armor of cells.

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It breaks down the armor of cells. And, when the glycocalyx is shed, what it does is it causes a pro-inflammatory response.

So, whenever the glycocalyx is shed in any and all epithelial cells, it causes what are called pro-inflammatory cytokines, so, things like TNF alpha, interleukin-2, blah, blah, blah. It causes the cells to release these pro-inflammatory responses. And, that also increases intestinal permeability. It increases not just intestinal permeability. It increases permeability of the arteries. And, guess what? **[37:30]** If you want to have atherosclerosis or cardiovascular disease, the glycocalyx has to be broken down. You have to have a pro-inflammatory response.

So, this kind of brings full circle to the notion that whole grains are disasters for cardiovascular disease. Everybody eats them. It's like cigarette smoking. Everybody smoked cigarettes in the 50s. Everybody gets cardiovascular disease. So, the point is that we believe that gluten-containing grains that contain WGA in particular, tend to promote cardiovascular disease through pro-inflammatory responses.

Now, in support of this are my colleagues, Staffan Lindeberg's group, at the University of Lund in Sweden. And, what they have shown is that you feed animals high-grain diets, and it increases CRP or C-reactive protein. So, c-reactive protein is an inflammatory marker in cardiovascular disease. So, it's a big wide world. And, many, many other effects of WGA and grains upon our health and well-being that go far beyond celiac disease.

Dr. O'Bryan: Your reference to the glycocalyx in the vascular bed is exactly what we spoke of with the vascular biologist Dr. Mark Houston who validated what you're saying, also.

Dr. Cordain: He and I've spoken together over the years.

Dr. O'Bryan: Yes, yes. So, now we understand another mechanism, another piece of the puzzle where this inflammation comes from that initiates the cardiovascular disease process.

A couple of questions for you: Is glycocalyx also referred to as the bio-film?

Dr. Cordain: I think I've heard that term before. One of the reasons that it has not been recognized, it was very difficult to...In the 1980s, it was predicted. So, the glycocalyx has actually been stained starting in about the late 80s or early 90s. **[40:00]** So, they developed stains that could show it. And, then we developed other techniques to actually see it. But, it was predicted from the physics of bloodstream flow. In other words, it created resistance that couldn't have been predicted by the endothelium. But, because it settles down and it's this feathery carbohydrate, it was very difficult to detect.

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And, so, the classic books, probably guys your age and my age, we didn't know about it. And, we thought that the endothelium was naked, and the red blood cells were exposed to it. And, now there's an incredible literature starting to develop showing that in order for anything to get past the gut barrier or even get past the endothelium, the glycocalyx has to be disrupted.

So, that's kind of the new information. And, I think the practical side of that is that any dietary compounds that can get in to breach the gut barrier and get into the bloodstream have the potential to breach arterial glycocalyx.

Dr. O'Bryan: Have you found that there are any enzymes that are available out on the market for our consumers that seem to be more effective against WGA to help to break it down?

Dr. Cordain: Well, lectins, they all bind sugars. And, they all have specific sugar-binding capacities. So, we did that experiment about fifteen years ago. We actually fed rats high concentrations of WGA. And, then, we also mixed in a specific sugar that binds WGA. So, the idea is if you mix this sugar with wheat or WGA, then it can prevent WGA from interacting. But, that was a dumb idea. It didn't work. [Laughs]

Dr. O'Bryan: Well, there's no way to know that ahead of time until you try it! [Laughs]

Dr. Cordain: Oh, there wasn't. So, the rat still developed their autoimmunine disease. **[42:30]** It was a colleague, Fraser Scott from Canada. And, we actually did that experiment. It's kind of like the experiment with humans, we were in unchartered waters. And, he has a rat model of type 1 diabetes, which is an autoimmune disease. And, so, we fed the rats whole grains. And, they still developed type 1 diabetes when they were given this specific sugar that binds WGA.

So, the problem is that we did the experiment in vivo. And, in all likelihood, the sugar's concentrations were also being taken up by the gut and being hydrolyzed in the gut. So, it just didn't work. And, also, it probably didn't bind up all the WGA. So, it was kind of a simplistic dumb experiment. But, at least in theory, it may have made sense. And, I think there's still pills out there now that some companies are hawking to try to, if you want to have your wheat and your cake and eat it too, just take these pills. But, our animal experiment says that doesn't work.

Dr. O'Bryan: Yes. If one is sensitive to WGA, does that make them sensitive to other lectins? Is WGA a member of the family, and we can conclude that the entire family of lectins one may sensitive to? Or, is WGA unique in the family of lectins that it has a higher percentage of sensitivity in humans?

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Dr. Cordain: Well, our group is the only experiment that's ever been done in humans. Period. We have an N of one. So, we don't know. I mean, we have one experiment in which we, like I said, it's like Columbus sailing from Portugal to what he thought was Japan. We simply, don't know. We don't. This is all theoretical. We're assuming that it gets into plasma, and that it's bound by the receptors in all of these cells and dendritic cells. But, we don't know. We haven't done those experiments yet. And, it's going to take some time.

So, to conclude that sensitivity to one lectin begets **[45:00]** sensitivity to another, I think it's preliminary to make that statement. Now, however, having said that, I know that practitioners like yourself and others, you can probably notice that it in patients. Is that people that tend to have GI tract problems or sensitivity to grains tend to be sensitive to dairy. They tend to be sensitive to legumes. And, you know that anecdotally. It's like, if you get them off of gluten-containing grains and things clear up, they're pretty good. But, they still have additional symptoms.

And, so, practitioners can, by a trial and error and kind of elimination diets, you can test these ideas and see if it works. And, so, that's kind of the beauty of working in the trenches with real people as opposed to working in the ivory tower of academia is that you can test these concepts. And, if it works on people, then you can have successes. And, you can theorize what's going on. So, that's what I would say.

Dr. O'Bryan: Dr. Cordain, on a one to ten, ten is absolute, no questions asked, this is the law. One is maybe it's worth a discussion on occasion. If you were talking to your grandchildren about food selections for them, without doing any tests, just in general, first about wheat and as being exposed to wheat, how important is it that they consider avoiding wheat just in general, and, then, about lectins in general? Where would you rate these in terms of the general discussion out there?

Dr. Cordain: Well, humans don't have a wheat requirement. We don't have a cereal grain or wheat requirement. We can get by and do get by just fine without cereal grains or wheat. As a matter of fact, cereal grains dilute the nutrient density of the diet. So, if you decide to eat grains--wheat or corn or rice or any of the other common grains--they're cheap foods that allow humanity cheap caloric sources.

If you choose to eat those foods, then the nutrient density of your diet immediately is reduced. **[47:30]** We published this in numerous papers including *The American Journal of Clinical Nutrition*, which is the flagship journal for nutritionists in the world. We pointed out the obvious, that the king isn't wearing any clothes.

If you eat grains, the vitamin and mineral content of your diet will be reduced. So, the point is that they're inferior foods. So, why would you want to eat an inferior food, unless you couldn't afford not to? So, unfortunately most of the world's people now, we're at

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seven billion. And, the only way we could have ever gotten to seven billion is through grains. So, most of the world's people, particularly non-industrialized countries, which used to be called third world countries, they're entirely dependent upon grains for their caloric source. And, when you get more than 50% of your calories from grains, you typically develop many nutrient deficiencies.

So, I guess what I would say to my grandchildren is that, "There's no guarantees in life. You can only put the odds on your side. You may walk across the street and get hit by a bus. But, you ought to put the odds on your side. And, if you want to live a longer, healthier, happier life, and you can afford to do so, you're better off getting your carbohydrate sources from fruits and vegetables, which were the traditional carbohydrate sources that our species have consumed."

So, grains are really an inferior food and, one finally thought, Tom, is that when we think about vegans and vegetarians--these are folks that are very much reliant upon grains and legumes to get their calories--if you decide not to eat meat, it's almost impossible to get calories from celery, and carrots, and broccoli. So, you have to rely on nutrient-dense foods such as grains and legumes and maybe nuts.

But, the point is is that, if this is such a healthy way to eat, then if we look at the meta-analyses of vegetarians, that they don't do any better at all for all-cause mortality--that means all causes of death, cancer, heart diseases or whatever--than do **[50:00]** the general population. And, actually, in countries such as India and Pakistan where people are vegans and vegetarians from the time they're born until the time they die, they have some of the highest death rates from cardiovascular disease of any population in the world, and they die earlier.

So, what would I tell my kids is that, "If you can afford to eat it, try to emulate the diet of our ancestors, the hunter-gatherers: fruits and vegetables and nuts and meat and fish, as close as you can get it to the wild state."

Dr. O'Bryan: Dr. Cordain, if our listeners want to follow-up with some of your writings, first for the general public, do you have any books that you would recommend?

And, then, to our doctors and health care practitioners who are listening, are there any summary papers that you would recommend to them?

Dr. Cordain: Well, first off, I think that knowledge about health and well-being and nutrition should be free to the world. We shouldn't charge people for it. So, what I try to do at my website, all of my scientific papers that I've ever published are all available as free pdf downloads. Most of the information that we've spoken about here today, except for some of the details, are available through white papers at my website,

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thepaleodiet.com, and as free information in my blog. So, I try to make that information available to the world's people, to everybody.

For those that want to read about it, I've written five popular books. And, you can get those at my website. You can get them cheaper used at Amazon. So, those simply just kind of fill out the detail and make a bigger story if you're not a scientist and can't read the scientific literature.

So, yeah, this story needs to be told to the world. And, I think we're all in this together. And, we can make a much better planet if people would consider their genetic heritage and the foods that shaped our genome.

Dr. O'Bryan: Amen to that! Dr. Loren Cordain, Colorado State University, affectionately and respectfully considered the godfather of the Paleo Diet. Thank you very much **[52:30]** for your time today!

Dr. Cordain: Tom, thanks a lot! It's been a pleasure and I look forward to meeting you in Portland.

Dr. O'Bryan: I feel the same. Thank you. See you then.

Dr. Cordain: All right. Bye-bye.

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