Transcript from Thursday, May 3, 2012 Webcast:
"State of the Union:
A Live Chat with Gluten-Related Disorders Experts"

Participants:

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- **Stefano Guandalini, MD**, Professor of Pediatrics, University of Chicago, Chief of Pediatric Gastroenterology, Hepatology, and Nutrition University of Chicago Children's Hospital, Founder and Medical Director, The University of Chicago Celiac Disease Center
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To watch a recording of this Webcast, copy and paste this link into your browser: www.CeliacCentral.org/livechat/recording

Transcription:

*The following was transcribed using the best of NFCA's abilities. In the case of parts where the presenter is muted or their voice is too low, please note that "**inaudible**" is written. Please also note that the presenter's initials are referenced throughout the transcription.*

Alice Bast (AB): Welcome to the National Foundation for Celiac Awareness' 5th webinar and lifestyle series in 2012. In fulfillment of our mission to empower, educate and advocate, we are excited to bring you the top experts in the field of celiac disease and non-celiac gluten sensitivity. Here today, for our session on the "*State of the Union: A Live Chat with Experts on Gluten-Related Disorders*," I'm proud to introduce Doctor Stefano Guandalini, Doctor Alessio Fasano, and Melinda Dennis. We were having a little technical problem, but Dr. Guandalini is now logged in; Alessio Fasano is coming to us all the way from Italy – thank you Alessio for participating from Italy!

Each panelist will speak for 20 minutes and will touch upon topics and questions that were sent to the NFCA Team. You, as our educated community, are always eager to hear the latest and greatest on celiac disease research. If time allows, NFCA's Healthcare Relations Manager Kristin Voorhees will be taking one question per panelist towards the end of the talk. Happy Celiac Awareness Month everyone! And I'd like to introduce our first guest, Dr. Stefano Guandalini, Professor of Pediatrics, University of Chicago, Chief of Pediatric Gastroenterology, Founder and Medical Director, University of Chicago, Celiac Disease Center.

OK, Dr. Guandalini, it's a hot topic. Everyone wants to know the difference between celiac disease and non-celiac gluten sensitivity. Can you give us the latest and greatest and explain the difference between these two conditions?

Stefano Guandalini (SG): OK, Alice. I hope that you're seeing and hearing me well. There's maybe still some trouble here but I'm trying to manage my abilities here. I think I'm one of those who actually would like to know the difference between celiac disease and non-celiac gluten sensitivity because in reality we know very little about that. We know pretty well what celiac disease is. It's a condition rather well-defined after decades of intense research and now we know it's an autoimmune condition triggered by the digestion of gluten and related prolamines that are found in gluten (wheat, barley and rye) in individuals who have a genetic predisposition. The disease causes a destruction of the intestinal epithelium, and with this a number of consequences, which can be very different from patient to patient. We know that the disease is also associated with a production of specific so-called celiac antibodies, which are unique to this condition and help enormously in our screening and diagnostic abilities. All of this we do not know about gluten sensitivity. We don't know the prevalence. We don't know what marker can be defined in gluten sensitivity. As a matter of fact, right now, they are to say that there is absolutely no biological readout that is no way can this diagnosis can be supported by any laboratory investigation. No antibodies in the blood are specific enough, or sensitive enough, for this condition. No antibodies in the stools can be utilized to diagnose or screen for this condition. Nothing in the blood can be done, and even the biopsies by definition of gluten sensitive individuals are normal. We do know that this entity exists. We have no idea what's causing it. It may have to do with a disorder of the immune response to gluten. This is likely, but it's not entirely clear to be frank with you. Recently Alessio and I were in Florence and we both heard Dr. Schuppan proposing as a major responsibility for gluten sensitivity actually proteins different from gluten. So we don't even know if it truly is gluten. He was claiming that there is this new protein called ATI or amylase trypsin inhibitor that is localized along with gluten in wheat that actually may be responsible for triggering an innate immune response in individuals, and especially gluten sensitivity.

But even if it is gluten, as I said before, we really lack biological readouts; there are no genes that are specifically associated with this condition. As I said before no antibodies, no other markers, and biopsies are normal. So we have to rely entirely on the patient history. Of course this should be corroborated whenever possible by a period of gluten withdrawal to see that whatever symptoms are thought to be dependent on gluten subside and a gluten challenge to see that they reappear. In the best ideal world this should be conducted in a blind fashion so that the patient wouldn't know whether or not they are exposed to gluten. Because unfortunately with this condition, studies have shown that often times patients who believe to be gluten sensitivity once challenged in a double-blind placebo manner are found out not to be. So, it's a cumbersome process until Alessio or someone else finds a biological marker, which is reliable for this condition, then we will have to rely on patient's history essentially.

This is not the case for celiac disease where we know a lot about this condition.

Alice, do you want me to go on about celiac disease and its definition, etc.?

AB: We have a question from the audience and one of the questions is on the increase. So if you're going to go on about celiac disease, then the audience would really like to hear.

SG: Again, I can't hear you very well, but I assume that you have asked me to go on talking about celiac disease, what constitutes celiac disease, and what is new in the way we think of it and diagnose it. So I'll carry on and you interrupt me when you want.

So essentially this condition, as I've said, is an autoimmune response to the ingestion of gluten that is trigged in genetically predisposed individuals. The new definition that the European Society for Pediatric GI and Nutrition has come up with a couple of months back, I think is worthwhile considering because it changes a little bit the way we look at this condition. They are now saying that in addition to being an autoimmune condition being triggered by gluten in individuals who have some specific genes, namely HLA haplotypes namely DQ2 and DQ8, this condition is characterized by a variable combination of elements. One of them being the celiac antibodies, the other being the presence of clinical manifestations, and the other being an enteropathy. So, in other words, we are now shifting our focus from a disease that had been considered for decades necessary involving an enteropathy with a consequent malabsorption to a condition that is actually a systemic disorder, autoimmune disorder in which the enteropathy is part or could be a part, so not necessarily is a part, and this is best exemplified by what we define potential celiac disease. It's a very interesting category of patients who do have the genetic background of celiac, who do have the celiac antibodies in their blood, who may or may not have symptoms, but who do have a normal biopsy. Those of us who are digging in the histology of celiac disease know that there is a spectrum of evolution of the intensity of the damage that goes basically from normal, with only an increase in intraepithelial lymphocytes that experienced pathologists can detect, all the way to the flat mucosa that in the 70's and 80's, we thought was the landmark of celiac disease. So in other words, the enteropathy may or may not be present.

In terms of prevalence, studies around the world are showing that the prevalence seems to be around 1% and it also seems to be increasing. We have data supporting doubling its prevalence every 20 years or so. Currently it's estimated to be around 1%. I know that Peter Green and his group has actually presented an abstract to the next DDW in which they have accessed to the NHANES ***(inaudible)*** blood samples of more than 7,000 individuals and they have confirmed what the previous study that was led by Alessio, to which we were a part, shown in 2003, basically a prevalence study of once again 1%. His data is also interesting because they were able to show that about 85% of those who could be considered to have celiac disease based on clearly positive blood levels of specific antibodies actually were not diagnosed. So that's quite interesting.

In terms of diagnosing celiac disease, we also have some news. Let me try seeing whether putting my headphones on might help. Just give me one second and I will tell you all the new findings you need to know about diagnosing celiac disease.

Alright, I hope you hear me better. Alright, so what's new, again I'm referring to the European Society for GI Task Panel who came out a couple of months ago with evidence based guidelines that are supposed to replace the old ones that I led in performing and in publishing 20 years ago. Basically, what they are currently saying is that if you have, now they are referring to a child, I must underline that, nevertheless, as the old diagnostic guidelines that ESPHGAN proposed in 1990, I think the new ones can also be considered adaptable, so to speak by adult gastroenterologists. But anyway.

So, a child who has symptoms suggestive of or consistent with celiac disease, now they may be gastrointestinal, they may be extraintestinal, who also has a genetic compatibility with this condition. So HLA-DQ2 or DQ8 present, will have to be tested for tTG, which is the most

sensitive antibody test we currently have for celiac disease especially above the age of 2, and if the levels are positive then we have a dichotomy. If the tTG antibody positivity is very high of more than 10 times the normal. So for instance if you have the usual cutoff in most laboratories in the U.S. nowadays is about 20, so you have to have 200 or more, well then in that case you need to check the more specific anti-endomysial antibodies (EMA). I do love the EMA because their specificity is so great. And in fact this evidence based paper supports that concept. They are saying if the antibodies, the EMA, under these circumstances, so let me recap:

Somebody with symptoms consistent with celiac disease, somebody who has genetics consistent with celiac disease, somebody who has tTG extremely elevated of more than 10 times the normal limit, and has a positive EMA, then under this very clearly defined and selective circumstances you may skip the biopsy. Because at that point in time the possibility of this subject having anything else other than celiac disease are extremely, extremely dim. Basically almost zero.
In all other circumstances, so when the history is not so clear, when you do not know the haplotypes, or when the tTG elevation is not as skyrocketing, then the usual process is to refer the child to a pediatric gastroenterologist and have this person assess the child and conclude diagnostic workup by performing the intestinal biopsy remains mandatory. They also are saying that for everyone who is without symptoms that belongs to an at-risk category, for instance first-degree relatives of patients, persons with Type 1 Diabetes, Down syndrome, etc., these individuals for them they do not suggest the possibility of allowing the doctor to skip the biopsy. They always should go through the itinerary of having the biopsy done. And then according to the results of the biopsy, as now many sources are saying, you can rely on the biopsy to classify this patient in potential celiac disease , meaning the biopsy is normal or only slight changes but no real villous blunting, in this case you are potential celiac, with or without symptoms mind you once again or you have full-blown celiac disease. Now, all celiac patients who –

AB: Dr. Guandalini, thank you so much for that.

SG: Sure.

AB: Several people have written in with questions about their risk of developing other autoimmune diseases after they have already been diagnosed with celiac disease and on the gluten-free diet for a number of years. Can you please speak to the intersection between celiac disease and other conditions, both autoimmune and non-autoimmune diseases, that are often discussed as being linked? One person specifically asked about Crohn's and auto-immune hepatitis.

SG: Alice, I will try to answer that. Again, I heard bits and pieces of your question, so I thought grasped the question but if I am not then try to correct me. Basically the question is whether there are connections between celiac disease and other autoimmune conditions, especially celiac and Crohn's disease and autoimmune hepatitis. So if I understood correctly then the answer is yes. Celiac disease, being an autoimmune condition

Kristin Voorhees (KV): I'm getting a message that your volume is cutting in and out so I think that we should move on to Dr. Fasano.

SG: Ok, I will be here. I will follow-up. I will be available.

KV: Dr. Guandalini, I apologize.

SG: That's OK.

AB: Dr. Fasano, you have been at the forefront of the research on the spectrum of gluten-related disorders, in particularly non-celiac gluten sensitivity. We are excited to be going right to the source and speaking with you today. What updates do you have for us?

Alessio Fasano (AF): You heard from Dr. Guandalini that gluten sensitivity is the last on the block, so we know very little. As a matter of fact, in the very beginning, I was skeptical of the existence of any such entity since we have always been taught that the reaction to gluten equals celiac disease and there are very few other people that have a reaction that is an allergic base like wheat allergy. You know, we see mainly adult patients in our Center for Celiac Research in Baltimore and therefore probably may be experiencing more for example, say at Stefano's center, to this growing number of individuals that came to us with these symptoms that really overlap with celiac disease, that really excluded it as a diagnosis, and we told them: "Look you know, definitely there is nothing wrong with you and we have to look for other reactions, you know other reasons for your symptoms. And in time, these people eventually keep coming back to our clinic saying I did exactly as you suggested but we can't find anything wrong with me and when I was on a gluten-free diet my symptoms went away, but at the same time it's really ***(inaudible)*** that our C enter for many years now back in Naples that Dr. Sapone really started to look very clearly and focusing on this new entity. It brought to our attention that indeed something probably was happening and therefore we started, really in the past two or three years, to look very closely at gluten sensitivity. Is it possible to have this entity, and sure enough, as Dr. Guandalini already mentioned, I believe that everyone who belongs to this entity exists, but as Dr. Guandalini explained when the only way to make a diagnosis of gluten sensitivity is by exclusionary criteria since we do not have tests that will point in that direction. And that's where our current efforts are all about. Now that we understand that it is a different entity we want to make sure that we can eventually identify the biomarkers for this condition, and we're doing a double blind study to identify the biomarkers that will eventually fill the gap that Dr. Guandalini was alluding to.

AB: A lot of patients are confused by the actual differences at the molecular level. They want to know – in plain English - what's the difference between celiac disease as an autoimmune disease and non-celiac gluten sensitivity as what I think you have referred to it as "an innate immune response"?

AF: Sure, sure, and again this is a very complex concept that I will try to make as simple as possible. There are two branches of the immune response. One is very genetically engineered, a long time ago shared by many animals of the animal kingdom that is sort of an urgent and immediate response to danger. So it's a response that will happen right away but cannot be sustained over time and that is called innate immune response. It just really responds to danger soon when we are exposed to it. If this danger is serious, let's say an infection and it doesn't go away, it means the immune system cannot support that response for too long and has to go for a ***(inaudible)*** calling the adaptive immune response to come in to help. The adaptive immune response system is a much more recent ***(inaudible)*** than the innate immune response and is much more sophisticated because it can customize weapons against enemies that we call antibodies. But to do so it takes time and therefore it's not good for immediate response. So if called upon by the innate immune response system for ***(inaudible)*** an enemy that doesn't go away, the adaptive immune system comes in and customizes a response and will take over for the long-term. Now, in the autoimmune diseases, including celiac disease, both the innate and adaptive immune system are involved. As a matter of fact, it's appropriate that the adaptive immune system that target

response rather than against the enemy, against itself, that causes the autoimmune insult. For example, the damage that is typical in celiac disease and this miscommunication between the innate and adaptive immune system that is responsible for the autoimmune insult. The major difference between celiac disease and gluten sensitivity from what we know so far, and again these are preliminary data because for me this is déjà vu. We are where we are for gluten sensitivity now, where we were 20 years ago with celiac disease. There are the skeptical, the ones who do not believe, there is confusion namely about where we should be when we don't know too much. But from what we understand in gluten sensitivity only the innate immune system, this innate response is involved but not the adaptive immune response. That's the reason why there is no ***(inaudible)*** for HLA-DQ2 or DQ8 involved like celiac disease and that's the reason why there is no autoimmune damage of the intestine typical of celiac disease.

AB: Are you putting together a prevalence study for non-celiac gluten sensitivity like you did for celiac disease?

AF: Well, as Stefano noted, we don't know if it's the real entity.

Red flags! They can help us really pick these people with gluten sensitivity out of the crowds. And that's what we're doing right now. It's a multi-center study, double blind that will identify the probable biomarkers. Are we at that point f and when we are at the point, if we can identify biomarkers or a biomarker, there may be more than one, then we can engage and embark on an epidemiological study to go from an estimate that we have right now that is roughly between 4 and 6% are the real numbers. Now keep in mind there is a state of confusion so great that if you go and Google gluten sensitivity prevalence you see numbers that go everywhere from 2% to 90 plus percent. Supposedly there are experts in the field who believe that we all have gluten sensitivity. Of course this is not credible, and if this is not credible then it does not exist. A concept that I believe everyone is now severing, and that's a reason why this is like déjà vu for me, number one we start to discuss about celiac disease in the U.S. there are a lot of people that are skeptical.

AB: Can you explain a little bit more about the difference between wheat allergy and non-celiac gluten sensitivity?

AF: People in the United States that will consume a gluten-free product. These can be divided into two categories. People that are occasional consumers; in other words, people that change diet to stay healthy so that maybe today they are on the South Beach Diet, tomorrow the Paleo diet, and then the day after to the gluten-free diet. They drive most of the market. And then there's the ones here, the ones who we are doing this webinar discussion, they are on the diet because of medical necessity. And here, we have three subgroups. The ones that react to gluten and/or the other components of wheat with an allergic reaction. These are the people that have wheat allergy. You can develop allergy to wheat like you can develop allergy to strawberries or shellfish. And here the numbers average, .2% to .3%, so ¼ or 1/5 of what is compared to celiac disease. They are a little bit more prevalent in kids than in adults, and that means that over time you may eventually grow out of it.

Then there is the autoimmune response to gluten that was amply discussed by Dr. Guandalini. That is celiac disease, which affects about 1% of the general population.

And then there is this third form that is gluten sensitivity that again, we don't know yet what kind of response, probably it is an innate immune response, we don't know indeed if it's against gluten or other protein components of wheat, and we don't have biomarkers for it.

AB: Inaudible.

AF: I think that again, to answer your question, studies like the ones we're doing right now mainly in Italy coordinated by the Naples Center, and in which we will be in charge to indeed validate these biomarkers of a list that is yet to be completed because if you do a study in which you take all-comers and some of these people can't respond because of the placebo effect you will not be able to really validate the sensitivity and specificity of this biomarker. But once we complete this double-blind study, then we can really have weapons in our hands to maybe move on. I think that since we start this study already and we are roughly at 1/3 of the people that we need to recruit to reach statistic significance, I will anticipate that probably within a year we will have this biomarker available.

AB: Inaudible.

AF: This partially relates to the question that you asked previously to Dr. Guandalini that probably we weren't able to hear that goes visa vie to answer the other question, "Why are we in the midst of an epidemic of celiac disease? You were mentioning the study from Dr. Murray. We did a similar study on a single cohort, so the same people over time and realized that there were people for 70 years for example who were able to eat gluten and tolerate it without having a problem and then all of a sudden they lost this luxury to tolerate gluten, the switch from tolerance to immune response therefore celiac disease. That brings about 2 key questions: What kind of tricks have they been using to tolerate gluten and not gotten sick with celiac disease? That would be the holy grail of preventive intervention for autoimmune diseases. That would be a premise on which would be extremely complicated. But we start the journey to answer this question.

The second question is what happened to these people that they lost that luxury? What happened to them that made them lose their tricks to tolerate gluten? And here the question is open to several of non-mutually exclusive explanations, including the quality of gluten that is ingested, the quantity of gluten that is ingested and the time of the introduction of gluten. Here, there are two schools of thoughts.

One that says that if you introduce gluten at a specific window of time between 4 and 6 months of age that can help minimize the risk of onset of celiac disease. We know that the introduction too early definitely increases the risk. This was the result of a natural experiment that unfortunately happened a long time ago in Sweden where a famous formula company that remains unnamed tried to ***(inaudible)*** the market by introducing what they call a ***(inaudible)*** formula, 45 formula, in which at two months of age they recommended the consumption of formula 45 with gluten. The ***(inaudible)*** generation experienced an explosion of celiac disease that went from 1% to 8%. And when the co-respective CDC in Sweden realized the problem they retired the formula from the market and everything went back. So we know that too early is a problem.

Then there's been some controversy about what happened by the delayed introduction of gluten. Because there are two studies publishing the same time, one from Denver, Colorado and the other one from Germany. In which one, Colorado said well, even if you delay the introduction of gluten after this window of 4 to 6 months, you increase the risk. While this ***(inaudible)*** Germany, they

suggested this was not the case. Of course, both studies were limited by the number of kids that were recruited and the fact that these two cohorts were actually aimed at another autoimmune disease that is strongly associated with celiac disease, and that is Type 1 Diabetes. So we embark on a study with ***(inaudible)*** kids ***(inaudible)*** risk for celiac disease and we have two studies in parallel, one that started in Europe coordinated by the Colorectal Center for Celiac Disease Research's Dr. Catassi that recruited now, more than 800 kids. Now we are almost at 5 years follow-up and one thing is for sure, this was a study in which some kids were introduced to gluten at the right time between 4 and 6 months and another group delayed by 6 months and introduced gluten at 12 months. What we're seeing there, with one, there is no increased risk, and actually the delayed group showed no prevalence of celiac disease. That doesn't imply though that we have the rationale to recommend to delay introduction of gluten because there may be time that they will catch up with the other group and then at the end the results will be the same. But at least what we can say so far for what we've seen in that cohort the delayed introduction of gluten at least delays the onset of celiac disease.

We on this other hand have started another study here in which in the long term are trying to answer the question, "Can you delay gluten introduction ***(inaudible)…***So in other words, what can happen to you to lose the luxury of tolerance but also what are the tricks that you can use to tolerate and by doing that what ***(inaudible)*** in a similar study, double blind, in which kids were either exposed to gluten at 4 to 6 months or delayed until 12 months, but we also follow other patterns, particularly the composition of bacteria that live in us, the so-called microbiota, and we come up with some very interesting preliminary but yet intriguing results. One, that the microbiota of infants at risk for celiac disease contrary to normal ***(inaudible)*** does not mature as supposed to be. Two, that there are some bacteria that were not represented, particularly a strain that is called ***(inaudible),*** which help our immune system to lose tolerance against these enemies, like gluten, and therefore is tantalizing and intriguing to hypothesize the possibility that the lack of this bacteria do increase the risk of celiac disease. And three, most importantly, we found some biomarkers, i.e. some red flags, that come on months before the onset of the disease so now what we can do to expand this into a large, multi-center study in which many centers, including the Center directed by Dr. Guandalini will be involved to expand these numbers so that we can see if we can confirm this data in large numbers.

AB: Inaudible.

AF: Sure, and again, this has been visa vie what we just said. So when we finished and completed the human genome we realized that genetically speaking we are very rudimental. We are made by only 30,000 genes. Compared to the genes in wheat, there are 150,000, so 5 times more, we are really rudimental. So it is very difficult to explain all that complex the human kind, including the diseases that are afflicted without the understanding that we actually are the results of two genomes. One is the human genome, one that we inherited from mom and dad, one that is stable and will never leave us and if it is defective, for example, the genes that increase the risk for celiac disease cannot be traded in, will stay there. They are stable. And the second genome, this microbiome, that is a hundred times more in terms of genes expressed than our human genome. The microbiota changes over time and can change from individual to individual in the same individual over time.

What is interesting that several studies particularly from colleagues from Canada seem to suggest that the ***(inaudible)*** microbiota from our mothers who are born from vaginal delivery we inherited a "good" bacteria composition because she already selected worse-off probable bacteria to live in

peace so to speak. And when we inherited those bacteria then we are in agreement with our genes and therefore we favor tolerance so to speak. If on the other hand we are born by c-section we don't inherit this pre-selected microbiota ***(inaudible)*** in the hospital bad bacteria. And therefore this increases the risk of many autoimmune diseases, including celiac disease, as demonstrated by our colleagues in Canada.

AB: Inaudible.

AB: Let's turn our attention to the gluten-free diet. We're really excited today to have Melinda Dennis to give us tips on living and eating gluten-free since food is our medicine and that's what keeps us healthy. Hello, Melinda!

Melinda Dennis (MD): Great, great. Thanks for inviting me. So, I'll start off with why it's so important to have a consultation with a dietitian who is skilled in celiac disease in order to help us balance our gluten-free lifestyle. Whether you have non-celiac gluten sensitivity or celiac disease, which are our specialties here today in this webinar.

First of all, a dietitian who is skilled in celiac disease is going to be able to explain the gluten-free diet and the resources for living well. We don't have time to talk about all of that today, but I want to get specifically intro nutrients. We know that balancing our nutrient needs are incredibly important and we know that when we remove wheat, we're removing protein and fiber, B vitamins, vitamin E, iron and minerals. So we make up these nutrients in many different ways with a healthy balanced gluten-free diet, which includes what many people may now be familiar with – the Super Six, which are the alternative gluten-free grains. Amaranth, millet, buckwheat, soy, sorghum, quinoa and teff. We also know that we have to make up for adequate Calcium and Vitamin D, especially for those of us who are lactose intolerant or perhaps have a dairy allergy. Most of the United States is low or deficient in magnesium, which is also low in the gluten-free diet, can be found in black beans, and spinach, halibut, pumpkin seeds and nuts. We also know that iron deficiency is one of the number one presenting symptoms of celiac disease that is undiagnosed. And it's very important to get animal sources of iron as well as plant sources. For example, humanely raised and local red meats and chicken and turkey but also from vegetable sources such as from e enriched cereals, lentils, chickpeas, etc.

Now, one of the main reasons, one of the main things that we see in clinic here is when people start on the gluten-free diet, they may have to control this desire to overeat or overcompensate for things that they were missing. I certainly know that when I was diagnosed 22 years ago I was psychologically missing a lot of foods. So there's this tendency to eat more calories, but of course after the gut lining has started to heal on the gluten-free diet, people may tend to eat the same number of calories, which will actually ultimately relate to increased weight for some individuals. Certainly we see that in clinic here too.

Just because you have celiac disease doesn't mean that you can't have other co-morbid conditions, for example type 1 diabetes. We know it's very prevalent in this population. So someone with celiac disease and Type 1 Diabetes is going to be carbohydrate counting and we know that the gluten-free flours and grains, particularly the commercial products are low in fiber and high in sugar and carbohydrates so that has to be taken in to effect.

Now, let's say you have heart conditions. Most Americans have to pay attention to this, all Americans do, particularly those with cardiac issues, so that's another thing that we take into

account. Lower cholesterol levels are pretty prevalent in people who are undiagnosed with celiac disease. But again, once the gut healing starts, your cholesterol is going to rise and you have to pay attention like any other American would.

Then there are those of us that are at risk for nutritional deficiencies from additional allergies. So for example if you have an allergy to fish you may be deficient in Omega-3's and want to either take a flax seed supplement or consider other ways to make up those Omega-3's.

And finally, something that's very big in clinic is the new presence of fructose malabsorption, which is the inability to absorb a particular sugar molecule called fructose. It's a sister of sugar molecules that includes all of the FODMAPs, which are the Fermentable, Oligo-, Di- and Mono-saccharides and Polyols. It's a big long name for sugars that aren't absorbed well in the body and if someone has fructose malabsorption as well as celiac disease, they are actually going to do two diets concurrently.

Finally, a multivitamin is very important in this population. I don't see a single patient who can't benefit from a gluten-free vitamin and mineral supplement. Depending on their iron needs, iron may or may not be included. And, I think I'll stop right there.

AB: Inaudible.

MD: Sure, well it's very understandable that people will be using it interchangeably but they do have two separate definitions. Food intolerance occurs when the body lacks a particular enzyme to digest that food and an example would be lactose intolerance. So it's not an immune system mediated response and it's certainly not life-threatening but the symptoms can be very, very aggravating and annoying and disruptive, certainly. The person would then avoid that trigger food, and you would call, well we'll explain food sensitivity next.

Food sensitivity, its definition is very sort of an understudied area if you will. Generally it means that people have an unpleasant reaction to a certain food. Perhaps they would develop acid reflux or nausea or some abdominal discomfort. But again, it's not an immune system reaction. It does not always occur in the same way in the body. And then, just to clarify the third would be food or wheat allergy, completely separated and immune-mediated.

Now, celiac disease would fall under an immune-mediated food intolerance where we must avoid it of course for life.

AB: Inaudible.

MD: Certainly. So celiac disease you know it's damaging the lining of the small intestine. And for that reason those of us with celiac disease have intestinal permeability or otherwise known as leaky gut. That is one of the hypotheses around the increased number of, prevalence of, food allergies within the population and certainly food intolerance is on the rise as well. Very little is understood about why there is an increase beyond that, why there's an increased risk with allergies within celiac disease. But we're definitely looking at that issue. I think what's important here is to heal the gut as quickly and completely as possible because as Dr. Fasano and Dr. Guandalini had mentioned you know, in their studies, the intestinal permeability it can be one of the reasons for these increased sensitivities that we're seeing.

AB: Inaudible.

MD: So, specifically, if you're trying to…are you talking about a person who has been initially diagnosed with celiac disease, just right off the bat, a new diagnosis?

AB: Inaudible.

MD: Ok. So on…

AB: Inaudible.

MD: Sure, so initially when someone presents to the clinic with a new diagnosis of celiac disease, obviously a complete blood count will be done. That includes your hemoglobin and hermatocrit, which are your two iron levels. Beyond that we're also going to check iron and Ferritin levels. Certainly B-12 vitamins and absolutely your Vitamin D.

AB: Inaudible.

MD: Vitamin D is of course known for its bone health, but it's also known to help our immune system and also to help prevent colon cancer. It also helps to heal the lining of the small intestine so it's very, very important.

We also have the thyroid checked. And of course the tTG, your tissue transglutaminase. In many more cases now we're checking zinc. When you think of zinc you think of your hair, your skin and your nails. More often we're also checking selenium, which you can associate with an increased risk of infections. If someone is excessively fatigued and their iron levels don't account for this we're going to check carnitine, and we also occasionally check copper. If a person is put on therapeutic doses of vitamin D or iron or a lab is found to be low, we will absolutely check that again until it's normalized. And then once yearly is appropriate for these nutritional labs that I have mentioned unless something goes wrong or it's slow to resolve. tTG can be checked once every 3 months if you are tracking it down to its regular level. And once normal can be and should be checked yearly.

AB: Inaudible.

MD: Yea, it would be very legitimate panel for a primary care doctor to run what we've discussed. Absolutely, when you're first diagnosed with celiac disease and yes, yearly.

If we could just back up for a minute to the question about nutritional deficiencies and allergies to the initial question. I think it's important to re member that when you have celiac disease and a concurrent allergy you need to think about what that food is and what it provides to you and how you can make up for it. So, what's the alternative? In the case of cow's milk for example, cow's milk obviously gives us calcium and vitamin D and phosphorous and protein. So if you've got a dairy allergy or are avoiding it because of lactose intolerance, then you absolutely want to find an alternative for that. This could be done with labeled gluten-free hemp milk or soy milk, flax seed milk, there's sunflower milk now. You have to remember though that these are not high in protein so you're going to have to look elsewhere for that. Although maybe fortified and enriched with calcium and vitamin D. They are definitely lower in protein. This would be particularly significant for children and again, calories. You would need to make up the difference in calories there.

So, when you have an allergy you need to reach out, seek assistance and find variety and definitely consider gluten-free multivitamin mineral supplement and perhaps other supplements as well.

AB: Inaudible.

MD: Sure. Absolutely. Yeah. So, absolutely, the first thing of course is to follow the diet very, very strictly, as closely as you can. That's going to be the number one treatment still for celiac disease. You're definitely going to want your vitamin D level checked and take the appropriate amount. So, the lab to ask for is the 25-oh D. That's the lab for vitamin D and that will give you a good indication of what your levels are. You want it to be at least above 30, preferably above 35. Many people test their vitamin D and find that it's in the teens or perhaps even lower. If it's low you would want your doctor to give you therapeutic dosing of vitamin D, which is about 50,000 IU's a day. Excuse me – 50,000 IU's a week, for 6 to 8 weeks. And then re-test your vitamin D levels. So those are absolutely key. You want a healthy and balanced diet of course, without relying on fast or processed foods to give you your calories. You definitely want to make sure that your grains and your grain-based products are labeled gluten-free because of the risk of cross-contamination. And then in some cases you may be low in the Omega-3s if you don't eat a lot of deep water fatty fish. So omega-3s are a very, very useful source of gut healing and anti-inflammatory proactive food. And then finally some people will use probiotics. I use it in clinic for symptomatic relief of gas or bloating or urgency. It's very dependent on my patient's situation. I choose carefully among brands and among, per the patient's condition when I choose a probiotic. You can always use probiotic based foods like yogurt with live active cultures, preferably without sugar, sauerkraut, kimchi which is a Korean condiment, nato which is fermented soybean from Japan and those sorts of things for probiotics in your natural diet.

And finally, I would suggest, I'm sorry Alice, finally I would suggest just watch your stool, right. Stool can give you a lot of data on the health of your gut. In other words, if it's floating that's not a good sign. You're either eating too much fiber, which is not usually the case with our patients or perhaps you are still malabsorbing, which is common when you're newly diagnosed. So watch your stool. You want them to sink, you want them to generally be of uniform color and you don't want them to have, obviously diarrhea or constipation. Ideally it would look like a banana and be well-formed and you would be basically unaware of your stool after you've had it.

AB: Inaudible.

AF: So, this is where we stand right now. After the health committee was established to have a bipartisan law for food labeling and after we successfully lobbied to have celiac disease there, the law was passed in 2004. It was decided that the Food and Drug Administration was supposed to be charged with implementing the law. We are in 2012 and are unfortunately we don't have a final ruling quite yet. Mainly because it's been a long and ***(inaudible)*** debate on how much is too much. It is unfortunate that we are the last to reach an agreement, that everyone else in the world has been agreeing on the 20 parts per million as the appropriate cutoff. There are many studies from many groups that are undisputedly, you know, proof that this cutoff is safe for the vast majority of celiac sufferers. The other paradox is that there has been a debate in Europe for a long time, but not between 20 parts per million and 0 as some of the support groups would like to see here because zero is not obtainable, it does not exist in biology. But between 20 and 100 parts per million, in particular the Scandinavians support the concept because for years they used that cutoff

without problems. Long story short, I believe that the Food and Drug Administration now has all of the elements to make a decision. They've done it in Canada, they've done it in Europe, paradoxically they've done it in South America, and we're the last one, and hopefully we'll have some final words by the summer of beginning of fall.

The rest of the recording is inaudible.