Tricia Ryan: We're going to start off and I'm going to introduce Dan. So really, he is a preeminent nutrition expert and in particular in the area of celiac disease. And he is the Director of Clinical Research and also founding member of the Celiac Center at The Beth Israel Deaconess Medical Center in Boston, Massachusetts. He sees patients, conducts research, and is on the faculty of Harvard's Medical School.

Now, he has published, certainly, numerous articles and chapters, he speaks internationally on celiac disease, in particular, my comfort zone with Dan's work is the *Real Life with Celiac Disease* diet book that I've been lucky enough to reread again because it has a very friendly approach and educational approach to the issue of celiac disease, and it's pretty much everything you'd want to know from, it's a great resource guide. And he certainly has case studies, as well as a lot of detailed information. He worked with a dietician, Melinda Dennis, in creating this book and resource guide, and he's, certainly, being very active in the field of celiac disease.

Most recently, he has a very interesting program he's put in place with the CeliacSure Biocard finger prick blood test kit, and he's going to share a little bit about the direction and some possible outcomes of the study. You guys were great in submitting lots of wonderful questions for Dan and I to cover today, and a lot of them were about assessment and the pharmacist's role in counseling patients, things like supplementation, etc. So Dan, why don't we get stated and tell people a little bit about sort of your interest in the teleseminar, what we want to accomplish today, and specifically, some of the focus on the kinds of information you feel is very helpful for a pharmacist.

Dr. Leffler: Sure, so thanks again for having me. So celiac disease is really one of these emerging diseases. It's something that we weren't talking a lot about in medicine only a few years ago, but over the last few years, we've really been realizing how many people this illness affects. We are not doing as good a job as a whole as a medical profession at diagnosing and treating people.

So I was very interested to get a chance to do this teleseminar and really talk to, perhaps, a different audience than I generally get to speak with, most commonly gastroenterologists and primary care physicians are the only clinicians that hear about celiac disease, but really, there's plenty of room for all different health professionals in trying to increase our rates of diagnosis and doing a better job of taking care of really this vast number of patients that are out there.

Tricia Ryan: And so specifically, we will be recording this, I just want to emphasize that and providing transcripts, so people can take notes, but the other thing I will provide at the end of the call is if they have further questions where they can email us. But let's just talk a little bit bout the terminology because certainly, what's coming off and we see so many people eating a gluten free diet and celiac disease, maybe you can just clarify, like you did in your book, which was great, the difference between celiac disease and gluten intolerance and how you make some, I guess, distinctions around that.

Dr. Leffler: Sure, of course, and this is a very common question, and it really goes to the core of how the diagnostic tests work and why we use them and we're so, we tend to be pretty strict about making the diagnosis of celiac disease in a formal way when we can. So celiac disease itself is a chronic immune mediated disorder that manifests primarily by small intestinal damage, otherwise known as enteropathy, which usually also manifests with auto-antibodies, (antibodies that attack other parts of your body), the most commonly known one of which is to tissue transglutaminase.

So again, celiac disease is a chronic autoimmune disease that targets primarily the small intestine but can have manifestations almost anywhere in the body and occurs in people who are genetically predisposed. We can talk about the genes a little bit later, but we have a good sense of what genes you need to get celiac disease.

On the other hand, there's this condition of gluten intolerance, otherwise called non-celiac gluten sensitivity. There's been a little work being done to really define the best terminology and standardize it. But it turns out, and this is even a much newer realization for people in this field, that there's lots of people out

there who don't have the immune mediated component, that don't have any inflammation, they don't have any intestinal damage, but still will get significant symptoms with gluten exposure and significant improvement in chronic symptoms with removal of gluten from the diet. And so that disorder is, again, distinct from celiac disease, you don't have intestinal damage, you don't have formation of auto antibodies, but you can have symptoms that are very, very much the same as individuals with celiac disease.

And it may seem like well, why does it really matter is the treatment is about the same and the symptoms are about the same, but from all we can tell at this point, celiac disease is associated with a lot of extra intestinal manifestations, such as osteoporosis, vitamin deficiencies, even a variety of cancers, whereas the non-celiac gluten intolerance or gluten sensitivity really isn't, it's really primarily a symptomatic functional disorder similar to irritable bowel syndrome.

And so although the treatment may be similar, the prognosis and the ramifications for an individual are much, much different. So we do like to make a real confirmed diagnosis of one of those two disorders at the time of when patients present to us.

Tricia Ryan: And that was a great explanation of both of those, and I know we're going to go into the testing, but let me ask this question first. I have consumer research, in my computer, not on my desk, that says about 15% of North American households are now eating gluten free. There seems to be a lot of interest around this. Maybe my question is what is contributing to this? Is it foods we're eating, is it body, you're talking genetic, maybe a little bit of clarity around why all of a sudden, or just better diagnosis?

Dr. Leffler: Sure. I think there's been a couple of trends that have combined to really produce this explosion and interest in a gluten free lifestyle and households going gluten free. And one of those is that we're diagnosing a lot more celiac disease than we used to, but we're still probably only diagnosing 10 to 15 percent of the celiac population. But again, this is a huge number more than there were before. And a lot of times in a family it only takes one individual with celiac disease to get the whole household to go gluten free; it often just winds up easier that way. So you don't need everyone to be

diagnosed in order to make that change for the household, so that's certainly part of it.

On the other hand, again, this is a very new realization for us, but it seems that there's a lot of people out there who previously have just been diagnosed with irritable bowel syndrome who get significant benefit from going on a low gluten or a gluten free diet. And I think this is an area that there's a lot less known about, but I think there's potentially a big role for specific food restriction type diets in patients with chronic functional bowel disorders. I think the foods that you need to take away to improve patients' symptoms with what has been called irritable bowel syndrome may differ from person to person, but there seems to be a lot of people who respond to gluten.

And so a lot of people, even as they've gotten a work up that says they don't have celiac disease will at least try a gluten free diet based on recommendations of their friends or physicians or family members, and if it works for them and they're doing it in a balanced way, that's a perfectly appropriate way to manage their symptoms.

Tricia Ryan: And that sort of leads me, maybe, to the next question because if you, the irritable bowel syndrome, my little bit of research in that arena, is saying like 20 percent of Americans can suffer from that or North Americans, and then you've got this self diagnosis, because we read consumer magazines and you go, that's me, I've got that problem. So what is the implication, though, of self diagnosis and eating gluten free? Why are health professionals sometimes concerned with people doing that?

Dr. Leffler: Sure, so that's a great question. So one of the things that's really remarkable about celiac disease and really separates it from almost any other chronic inflammatory disorder is that once you treat it, it goes away, to the extent that there's no medical test we have that can separate out a person with treated celiac disease from a person without celiac disease at all. The intestine can heal up back to normal, the antibody test can normalize.

So once people are on a diet, it makes it very, very difficult to tell what they have or what they don't have. And again, most of these

people are on the diet because they have symptoms, so asking them to go back on a gluten containing diet, which often would require, basically, a regular diet, an equivalent of about four slices of bread for up to eight weeks, can really be a lot to ask of people. And there's a lot of resistance, for good reason, from patients asking them to do this gluten challenge to define whether or not they have celiac disease.

But again, I think it's important to remember that it's an important differentiation to make, again, for all the reasons I mentioned earlier on, but also because celiac disease is a hereditary disorder, 10 percent of first degree relatives, give or take, will have celiac disease. So if one person gets diagnosed, it, actually, has ramifications for everyone else in the family versus gluten intolerance or non-celiac gluten sensitivity, it can often just be that one person and there's no added risk to other family members. So it is very important, and I do really always try to encourage patients to at least get some initial blood work done for celiac disease before they start modifying their diet.

Tricia Ryan: So this does lead me into this diagnosis area, and we had a lot of really good questions because there are different kinds of testing procedures. We had people asking about people doing the scope versus the blood work versus using a product like the Biocard or CeliacSure testing. So maybe you can sort of define what the tests are for and what do they actually do because you said there's the genetic part, and then, of course, there's people with their self diagnosis with these things, the positive and the negative, and they may not all be clear. So where does this percentage, 96 percent accurate, where does it all fit in, Dan?

Dr. Leffler: Sure. So the modern serologic tests, and there's a couple of these out there, all can be sort of generalized to be about 95 percent accurate. Again, there's a small percentage of people, maybe 5 percent of people who have a positive blood test that don't have celiac disease, and a small percentage, about 5 percent of people with celiac disease, will never have a positive blood test. And again, the blood tests are markers of the disease; they're not the disease itself. That's not surprising.

And again, it's a much better test that what we have for almost any

other autoimmune disorder, if you think of diseases like lupus or autoimmune hepatitis and those type of things, the blood tests we have for those are not nearly as good as what we have for celiac disease. But again, they're not perfect.

So the modern celiac blood tests, again, are TTG, tissue transglutaminase, is the most commonly used one. The other really new one is Deamidated Gliadin Peptide, or DGP, a slightly older one, but also very good, but just limited a little bit by expense, is endomysial antibodies, or EMA. And the old test, which we used to be using, but really has very little place in modern celiac diagnosis, is antigliadin testing or AGA testing. Those really, in general, should not be used, perhaps with the exception of young children below the age of 2.

So all these tests are excellent, and again, in a typical patient, somebody with irritable bowel type syndrome symptoms, if you have one of these blood tests that's negative, a negative TTG on a regular diet, that's really all you need to do to rule out celiac disease in that person. It has a high enough negative predictive value in a sort of low gen moderate risk patient that you don't need to go further. On the other hand, anyone with a positive blood test, no matter what their risks, really should go forward and have definitive diagnosis made through an intestinal biopsy.

Tricia Ryan: And then with the doing the biopsy, which is one of the questions we had, since it's invasive and sedatives are needed, is this going to continue to be the ultimate test then?

Dr. Leffler: Well, I think for the time being, it's going to remain the gold standard. There has been some effort in pediatrics, primarily, to see if we could do away with the intestinal biopsy. You know, again invasive procedures are more of a big deal in children, obviously, than they are in adults. Endoscopy is, it's an invasive procedure for sure, but it is also a very safe procedure, it can often be done without any sedation. In fact, outside of North America, it's primarily done without sedation. It only takes a few minutes.

And again, there's two real benefits for it. And the first is really, again, really defining the diagnosis. Again, there are those people, there are 5 plus percent of people that have a positive blood test

that really don't have celiac disease. And to give them a lifelong diagnosis that's going to affect them and all their family members without taking that step is difficult.

The other thing, though, is that celiac disease is, again, a lifelong disorder, and that means that a lot of people, sooner or later, will have some problems. They'll have recurrent symptoms, they'll have some blood test problem, and they'll go back to their gastroenterologist or their physician and try to figure out what's going on. Having that baseline information about what their intestine looked like when they started can be incredibly helpful in driving that evaluation. So really, I think in adults the endoscopy and the duodenal biopsy is really here to stay. Although, in children I think it's an open question, and perhaps in the coming years, we'll see some alternatives to that.

Tricia Ryan: So then, still in that vein or spirit, there were questions around the blood work can be extremely confusing, and I'd like, and you do some great charts in your book, can you explain why someone having extremely high TTG and a negative EMA, could the TTG be a response of some other ailment or is it gluten related?

Dr. Leffler: That's a good question. So the blood tests, and for most of these, EMA, TTG and DGP, are fairly concordant, in that if one is positive, likely, they'll be also positive. In general, if you are going to have discrepancies, there can be a couple of reasons. Hemolysis, actually, probably the most common for blood testing, i.e. the red blood cells break during phlebotomy or something like that, that can cause a false negative TTG, but it shouldn't affect the EMA.

There are also a few disorders where you just get very sticky antibody levels, hyperglammuglobulin, these are primarily hematologic problems, some of them very benign, but just people's antibodies are just made a little bit abnormally and they can just stick to lots of different things. So you can have a high positive TTG but a normal EMA. So those are all possibilities.

The other thing that is, perhaps, the most common is that you just, when you have sort of one low positive and the other one is negative, and again, those are cases that could be just early

developing celiac disease, sometimes after an acute gastrointestinal infection or with severe liver or heart disease you can get a low positive TTG. So there's a variety of conditions out there. Again, which really just underlies the point of why we're still reliant on biopsies because no blood test is 100 percent accurate.

Tricia Ryan: Okay. So we could go on and on about that one and I know it's quite a complex subject, and certainly, looking at your book helped me with the little charts you had in there so I could get all of these different things sorted out. In terms of nutritional concerns then, with someone who has celiac disease, and I guess even if people are avoiding gluten and on a regular diet, is there a need to supplement? What nutrients are you considering most critical, and is this, perhaps, a case of where pharmacists can recommend supplements, which ones should they be looking at?

Dr. Leffler: Yeah, I think this is a wonderful area where pharmacists can be involved, and we know that nutritional deficiencies are very, very common in patients on a gluten free diet. And regardless of whether they're on a gluten free diet because they have celiac disease or because they have non-celiac gluten sensitivity or whatever, gluten free foods tend not to be fortified quite as routinely as non-gluten free standard foods.

So gluten free diets are often low in B vitamins, they're often low in iron, so our typical recommendation for every celiac patient include a multivitamin, and that with minerals according to age and need, as well as extra calcium and vitamin D. And we really like to see our celiac patients get a minimum of a thousand international units of vitamin D per day because of the high risk of osteopenia and osteoporosis in the population.

I would just say that the three most common nutritional abnormalities that we'll see in patients with celiac disease are iron, vitamin D and zinc, and zinc is really the one that most people may not think about, but zinc is really important, not only for immune function, but in hair and nails and skin, so a lot of our patients will come in with brittle nails, hair falling out, very dry skin, and a lot of it can be traced back to zinc deficiency, so that's one we are more routinely checking for and supplementing.

So really a gluten free diet can be an extraordinarily healthy diet if it's done correctly, but it needs some work, and most people need a little bit of supplementation on top of what they're getting through foods to really get them to the optimal health.

Tricia Ryan: You also, I thought it was fascinating, talked about magnesium, I think it was magnesium citrate, in the context of constipation because that, actually, came up a lot in your book and where people have typically thought of the celiac disease, and I know when I went through and studied nutrition, celiac disease was a childhood disease and massive weight loss and diarrhea. But constipation came up a lot, maybe you can talk a little bit about that.

Dr. Leffler: Sure. That is one of the more common things people will come to us with, and you can have constipation as a presenting symptom of celiac disease, again, which is counterintuitive. You would expect anything that causes malabsorption to cause diarrhea. But in a lot of people, especially in adults, what you find is that although they are malabsorbing to some extent, they can compensate for that. However, the inflammation and the damage to the intestinal tract leads to an overall motility abnormality so they can get a lot of bloating, cramping, they can get nausea and vomiting or constipation, just because the motility of the gastrointestinal tract isn't normal.

But even beyond that, once you treat the celiac disease, one of the most common deficiencies on a gluten free diet is fiber. So we'll put almost everyone on a fiber supplement, sometimes just prophylactically, knowing that a lot of them are going to go on low fiber diets and come back to us with constipation. So even if they don't necessarily need it right away, we'll sort of tell them, listen, there's a good chance you're going to be constipated once you go on this diet.

A good fiber supplement, especially one of the ones that doesn't product as much gas as others, the psyllium ones we tend to find produce a lot of gas and bloating, can be very, very helpful. And that's often all they'll need to regulate bowel movements. But it's a big problem and it affects well over a quarter of our patients at some point or another will be some degree of constipation.

Tricia Ryan: And I know you had great charts which showed the various fiber supplements and if they were gluten free and suitable, so that would be very helpful for the pharmacist as well because it is sometimes a challenge, I guess, with the kinds of things that they're recommending because I recently talked to a probiotic manufacturer and it was gluten free, but they didn't indicate that on their package and so this is something the pharmacist has to deal with, correct?

Dr. Leffler: Yes, completely. And in fact, that's one of the most frequent complaints I get from patients is trying to figure out which of their medications and supplement are gluten free and which they have to worry about. And these days when a lot of things are generic, things can switch manufacturers really without any warning. So I have all my patients, I try to get them to ally with their pharmacist and sort of develop a relationship because it's really, obviously, going to be very difficult for most patients to ferret out when there's been medication changes, when a manufacturer is changed and perhaps gluten is getting in.

And gluten in a medication taken on a daily basis is more than enough to cause significant intestinal damage and recurrence of symptoms and we've even seen a couple of patients over the years hospitalized for celiac related symptoms that were due to nothing more than a new medication with gluten in it. So it really is something to be very, very vigilant about, and unfortunately, although food labeling is sort of slowly coming along, the drug and supplement labeling is very, very patchy. And most physicians just won't be aware of this issue enough to help patients sort through it. And I think a pharmacist is perfectly placed to help keep people safe on the medications and supplements that they need.

Tricia Ryan: So you kind of answered my next question, which was about the inadvertent gluten exposure. So you're saying things like supplements, which are taken daily, there isn't a safe level, like it's okay to have this much. I know there's minimums that people talk about, but so what do people do, it's the pharmacist, any other resources that they have around foods that for eating out and being safe with gluten they are not really aware of being in a product?

Dr. Leffler: Yeah, so there's, in restaurants have started to really come around, driven by as much this non-celiac gluten intolerance population as they are by the celiac population. But more and more restaurants do have gluten free menus, or at least chefs that are somewhat aware and help prepare meals. It's still always a risk, though, it's always a burden for patients with celiac disease to go out. Most patients will wind up with their favorite restaurant, there's things that they can trust, places they know that they can go and the things they know that they can order.

But the sort of spontaneity that many of us take for granted in going out to eat or in socializing is really lost for patients with celiac disease to where they shop, what they eat, even the type of things they buy, medications and whatnot. Everything needs to be researched to an extent that just generally is beyond what people are used to doing. And this is part of the big burden of celiac disease that really persists for years and years when you talk to patients even a decade later when they've been diagnosed, you'd think they'd be pros and used to everything. They're still finding it's a significant hardship to continue the vigilance they need to keep a strict gluten free diet.

Tricia Ryan: So speaking of vigilance, now we have combining diets, and this is another thing, and this is, I think, where the pharmacist really plays a role if you take something like diabetes with celiac disease, and those two kind of come together sometimes, don't they?

Dr. Leffler: Yes. There's certainly an association between type 1 diabetes and celiac disease, but more and more, as we are seeing older individuals that are diagnosed with celiac disease, the average age of diagnosis for celiac disease, just as an aside, in America and Canada is about 40. So we're seeing more and more type 2 diabetes along with celiac disease just as an age related population demographic. And that's a difficult balance to hit.

And as much as any patient with either diabetes or celiac disease needs some expert help from a dietician, from their pharmacist, from their physician, the combination can be very, very tough to manage. And really, the extra support and guidance is really crucial to get them to manage both disorders effectively.

Tricia Ryan: So it leads me a little bit into our next one, too, because obviously managing your weight in diabetes and then managing weight, in general, for all of us, it seems like we're hearing reports all the time that we are overweight, so when people do go on to this gluten free diet, what are some of the main reasons for weight gain? And certainly, I'm sure consumers going to a pharmacist and are looking for those magic pills and things like that to happen, what kinds of sort of thoughts do you have around weight gain and things that consumers can do and not take special pills from the drug store that are not really suitable for people? But what's happening with weight gain in a consumer that has celiac disease?

Dr. Leffler: Of course, so this is a very common problem, unfortunately. In a study that we recently completed, we found that 20 percent of our patients move from a normal weight class to an overweight weight class after going on a gluten free diet. So that's obviously a huge problem and one that we take very seriously. So we've made weight counseling a part of our gluten free diet education program for all newly diagnosed patients now. At least being aware of the issue is the first step towards managing it.

One of the things we'll always do is we'll look at other medications that may be associated with weight gain, steroids, obviously, some of them have autoimmune diseases and will be on steroids, that will be a problem. A lot of the other diabetes drugs, as we were just talking about, are associated with weight gain. So we try to minimize any other aggravating factor that could lead to weight gain. But otherwise, we really try to stress healthy eating, exercise, the normal thing. I would stress, though, that one of the big symptoms of celiac disease, even more than gastrointestinal symptoms, is fatigue. And if we're telling people to maintain an exercise level while they're fatigued it's very, very difficult.

So fatigue is multi-factorial, there's lots of different reasons, but the two studies that have shown good effect in treating fatigue in celiac disease, one has been with B complex vitamins and the other one was with L-Carnitine supplementation, and both showed over about a six month period, you have improvement in some pretty recalcitrant fatigue symptoms, which is a big player in both overall health, weight management, and quality of life. So that's, again,

another place where a pharmacist can really play a role because there's these things that are very simple on paper to do, but they're just not, people just aren't aware of these type of interventions.

Tricia Ryan: And then the other thing, too, Dan, that a lot of the foods that are prepared to be gluten free tend to have a higher fat content, do they not, in order to make them sort of more acceptable, from a sensory perspective? So you can also be consuming twice the calories as a celiac patient when you're going from a normal bagel to a gluten free one, that also can be part of the, I guess, misperceptions about how healthy gluten free food can be.

Dr. Leffler: Absolutely. And even beyond that, we'll often see patients sort of feeling restricted and feeling deprived on one side, not able to eat what they want, so they compensate. So they can't have the roll they want with dinner, so they'll have an extra serving of dessert or something like that. So the compensatory strategies that people use to sort of cope with the gluten free diet can often be very counterproductive.

Tricia Ryan: But I'm going to skip my next one on kids and come back to it, but you do, actually, have a whole chapter on depression and anxiety. You talk about the health issues and how people feel, so there is an emotional connection and maybe you could chat a bit about that, sort of the way I compensate with the extra dessert because I can't have the bread.

Dr. Leffler: I think this is changing, but there has, historically, been an under-appreciation for the burden that celiac disease places on people in the medical community. Again, it's a chronic disease, and so all those emotions people go through with any chronic disease happen with celiac disease, everything from denial to being angry about it to trying to bargain their way through, saying, well, I'll eat some gluten free sometimes but I'll have that roll whenever I want it, and all these strategies are sort of normal parts of coping, but they are not necessarily helpful. And a lot of them people can get stuck in a certain phase of this coping.

And depression around not being able to eat what they want and not being able to go to that party or go on that trip in the same way they were planning to and also anxiety, never knowing if what you

just ate is going to make you sick. If you've got issues that really persist for years and years and so having as much support on all of the different levels, having someone that says, you know what? Don't worry about your medications, I've got them covered, or having a family member who says don't worry, we can go back to that restaurant because I know it's safe there, those are the type of things that can really make a big impact in people's lives with celiac disease and help them cope with a lot of these things, the depression and anxiety that are very common.

Tricia Ryan: And then, so people then ask a lot of questions about children, too, and so are there special ways that they're diagnosed and are there special nutrition adjustments that are required for kids and celiac disease?

Dr. Leffler: So in general, children and adolescents are diagnosed and treated in exactly the same way as adults. The one area that is a little bit different is very, very young children under the age of 2. Again, thankfully, celiac disease is fairly rare in that age group. But in children under the age of 2, none of the blood tests are as good as they are when you get older. The immune system just isn't as developed. So in those cases, there are much more reasons to do antibody panels where you'll check the old antigliadin, as well as the TTG or an EMA to see if anything is cropping up as positive because, again, you just don't know how the immune system is going to be reacting at that stage.

Otherwise, the diagnostic tests and the algorithms are basically the same for children and adults. The only thing is with children, again, we have growth and development to contend with, so we're much more vigilant about diagnosing children, especially with those with first degree relatives or other autoimmune diseases, like type 1 diabetes who are at risk of celiac disease, we test them much more frequently.

And we monitor them much more closely to make sure they're hitting their growth curves appropriately and that their blood tests, that their celiac blood tests are normalizing in the way that they should. Again, with adults, we'll allow a little bit more leeway because those major parts of life are out of the ay. But our fear is with children, if they're not treated aggressively and completely,

they could lose growth and never really get it back.

Tricia Ryan: And then we talk about how strictly you do have to follow the gluten free diet, and you've mentioned the bargaining, and is there safe levels of gluten? And why is it important to be careful? Like do the villi come back and get healthy? Am I okay? Can I get reprieved? Will I grow out of this disease? Those are all sort of the kinds of thoughts or questions.

Dr. Leffler: So there's different answers to different aspects of that. So yes, the intestine does heal, again, that's the wonderful thing about celiac disease, our intestine will heal back to basically normal, in many cases, although it can take a while. But recurrent gluten exposure will damage the intestine again, and once you have it, it is lifelong. Your sensitivity, in terms of symptoms, can wax and wane over time, that's the same for almost any inflammatory disorder, but the intestine will be damaged at any point in your life with gluten exposure. And so once you get it, you have it for life.

In terms of a safe amount of gluten to get in, that's really a hard thing to say. There have been studies that have shown that in the 20 milligram per day range, which is basically equivalent of a few crumbs of bread, is basically safe. But if you push that up to 50 milligrams a day, which is, obviously, a few more crumbs of bread, it's enough to damage people's intestines. So these are teeny, teeny amounts of gluten we're talking about.

But the one thing that makes answering that question really difficult is that there's really no such thing in our culture and our environment as being 100 percent gluten free. There's gluten in the environment, there's things that people are exposed to every day. So even in these very tightly controlled studies where people with normal blood tests, oftentimes, their intestine is not fully healed and our best guess is that there's teeny amounts of gluten that can get in on a regular basis to everyone, no matter how strict they are.

So that's, for a large reason, sort of one of the reasons we say to be as strict as you can because we know no matter how strict you are, it's never going to be a zero gluten diet, there's just no such thing in this world, unfortunately.

Tricia Ryan: And then, of course, there is bone disease and skin disease or skin conditions that are associated and related to celiac disease. There are certainly two sort of complications that we have to watch and monitor for. So what role, again, can the pharmacist play? And we did have a question about people being diagnosed with the dermatitis and I know, I guess, the pharmacist can talk about the creams that they would possibly recommend, but does this go away when you adhere to the gluten free diet? There were kind of questions in that camp as well, so maybe you could talk a bit about that.

Dr. Leffler: Sure. So let's tackle the skin conditions first. The most classic skin condition is dermatitis herpetiformis, this is a blistering, very itchy rash that occurs mostly on the extensor surfaces, the elbows, the knees, legs, the back of the neck, and it can really be a disabling rash, very, very itchy. It does respond, basically, completely, to gluten free diet. But that can take an awful long time. And for many people, some supplements, especially in the beginning of treatment, are necessary to get it under control. The most common medication is Dapsone that is used.

Dapsone, obviously, has side effects, neuropathy, aplastic anemia would be the two most common, so it does require monitoring, but it works extremely well. It doesn't do anything to the underlying disease, it just stops the inflammation. So the goal is not to use Dapsone to treat DH permanently, but just to give you enough, people enough time to be on the gluten free diet that they can heal themselves and wean themselves off Dapsone.

Again, there's a couple of other things beyond just gluten, certain other things like high iodine consumption, actually, can worsen dermatitis herpetiformis. So that's another place the pharmacist can really be involved in seeing there's anything they're taking in medications or supplements that could be responsible for recalcitrant dermatitis herpetiformis.

Tricia Ryan: So that's as simple as what's in salt?

Dr. Leffler: It can be. Usually the amount that you would get in table salt isn't generally enough, but it is in some other supplements or

medications or some people who eat a lot of seaweed actually can get enough to cause a flare of their dermatitis herpetiformis. It's important to know that in general, topical preparations, in general, will be helpful for the itching of dermatitis herpetiformis, but cortisone creams and those types of things that we would use for most rashes won't be that effective for dermatitis herpetiformis. So a topical cream can be very helpful for the itching, but they won't make the rash go away in the way that you would see for eczema or psoriasis, for instance.

On the other hand, most of the time, people get very worried about gluten in all things, topical, usually, even for people with dermatitis herpetiformis, you really need to ingest the gluten to have the autoimmune reaction, so gluten in shampoos, gluten in creams and things like that really isn't a big deal for the vast majority of people.

To finish off some skin conditions, while dermatitis herpetiformis is the classic condition, it's been shown in nine studies now that many other skin conditions, including things like eczema and psoriasis can actually be worsened by active celiac disease, whether this is a nutritional problem or whether this is due to just general autoimmune inflammation we don't really know. But again, flares of those other types of skin conditions can suggest that people with celiac disease isn't as well under control as it should be and may suggest the need for repeat blood testing or further evaluation.

Bone density was the other thing that was brought up.

Tricia Ryan: Sure, uh huh.

Dr. Leffler: Bone density is one of the most common extraintestinal manifestations of celiac disease. Osteopenia and osteopororsis together are seen in about 50 percent of adult celiac patients at diagnosis. Again, that's one of the reasons we put everyone on at least some vitamin D, no matter what, and we'll also check vitamin D levels to try to titrate to the right level for that patient. It's also recommended that every patient get a bone density study within the first year or so after diagnosis.

Oftentimes, there's great improvement in the bone density once you treat celiac disease, so many patients, fortunately, aren't going to need a bisphosphonate type of medication for their bone density, the gluten free diet can be enough to get them back on track. But we do want to follow this very closely.

Tricia Ryan: And in terms of resources, I can certainly say to our audience that the reallifewithceliacdisease.com is the website where your book is and the resources that maybe you could just outline maybe for the pharmacists a couple of good places or resources that would be helpful for them, in terms of sites or things like that to get more information on some of the conditions we've talked about.

Dr. Leffler: Sure, so in general, there are, the main website, the main organizations that have put out really good information on celiac disease have been the patient led group. This is in Canada the Canadian Celiac Association, CCA, is excellent. In America, the NFCA, the National Foundation for Celiac Awareness, Celiac Disease Foundation, CDF, Celiac Sprue Association, CSA, all of those have excellent websites.

And the other one specific to pharmacists, which I recommend all the time and is really an excellent site maintained by a pharmacist out of the University of Ohio, is glutenfreedrugs.com, Steve Plogsted really does a very nice job of keeping a fairly up to date and extensive list of medications that are gluten free. And this is something that I try to have all my patients keep at their fingertips as a resource.

Tricia Ryan: That's an excellent one, that's great. Now, you're embarking on a very interesting study with CeliacSure and their test kit for the first and second degree relatives or family members, you've certainly made reference a little bit earlier in our call to the fact that I might be diagnosed and then my children or maybe my parents, etc, maybe you can talk a little bit about your program and sort of what the goals are in doing this testing or study.

Dr. Leffler: Yeah, so I guess there's two things just to remember going in is that first of all, celiac disease is sort of greatly under diagnosed. We're diagnosing 10 percent probably in that range of patients out there who actually have celiac disease. So we're not doing, as a

medical community, a great service to patients. And even in patients who do get diagnosed, and they're, on average, reporting about ten years of symptoms prior to diagnosis, this has been remarkably similar in a Canadian survey and in an American survey out of New York City from the Columbia group. So patients are getting a diagnosis that's very delayed or not at all.

The risk is also of celiac disease is much higher in relatives of patients with celiac disease, so where as it's about 1 percent, in general, of the American and Canadian general population, it's about 7 to 8 percent of first degree relatives and about 4 percent in second degree relatives, so you have a very much enriched population. It doesn't necessarily mean we need to screen all adult relatives, there's no good evidence for that, but it does mean we really have to keep our radar up for celiac disease in these individuals.

One of the things, because we do such a poor job, in general, diagnosing everyone out there with celiac disease, and it's just been hard to reeducate all the medical clinicians out there about celiac disease and who they should test for it and how, I was very interested to see sort of a direct consumer based test out there, new ways to get people diagnosed, ways that people can really control their own diagnosis is say maybe this is me, I should get blood tested or I'm about to go on a diet, but I know I'm supposed to get tested first, but my primary care physician is unavailable or isn't interested in testing me.

So it was very interesting in seeing how this new finger stick test could be used by patients to help diagnose them, and hopefully on a much broader scale one day to increase the proportion of patients with celiac disease who actually get a prompt and accurate diagnosis. So what we've been doing is giving out the kits to patients, who are actually patients of ours, to give to their relatives, first or second degree relatives, who haven't yet been tested and aren't on a gluten free diet, to see if they can use the test at home by themselves, to see if they can interpret it appropriately. Again, this is not for diagnostic use, at least in the United States, and it's not diagnosis by itself, but it's a good step in the right direction.

And we've given out a couple hundred of these tests already, and

people have really done very well with them. They tend to be able to make it through, to use the test appropriate, to interpret it accurately, and so I'm very excited to see once this starts to get use don a larger scale whether this can really start to chip away and improve our diagnosis rates in North America.

Tricia Ryan: So one of the goals, then, of the study is that are you finding, like I read in your book, sometimes family members find out and they don't want to test, and especially if you have to make an appointment and see the doctor, is this sort of facilitating some ease that way, as well?

Dr. Leffler: Yeah, what we're hoping is that the use of this test isn't going to be an end all for the patient, especially if it's positive. But even if it's negative, if they have persistent symptoms, but again, I hear all the time in the clinic, I would have gotten tested, but it just was so inconvenient, so I just started to go on the diet on my own and now I feel great and now it's really hard. This is just going to be a much lower resistance pathway to getting people tested on their own. And again, this finger stick test seems to be just as accurate, in general, as the normal laboratory based blood test, and you get the result right away, basically. And it can be used –

Tricia Ryan: Ten minutes or something?

Dr. Leffler: Yeah, and people like that feedback, and it's nice for clinicians, as well, to be able to give people information right away, rather than take the blood and have them come back or call them back a week later. So I think there's a lot to be gained by having an accurate point of care test for celiac disease. And people are very interested in it, the people I've talked to, they're interested in using it and seeing how it works, seeing if it can help them make sure they're keeping a strict gluten free diet. And I think all these things are perfectly appropriate uses of the test.

Tricia Ryan: So then the pharmacist's role in something like recommending the CeliacSure kit, given the way that you've been talking about it, how can we put it in context for them?

Dr. Leffler: Sure, so there are two obvious places to use it. One is a person who has chronic gastrointestinal symptoms, diagnosed with

irritable bowel syndrome, those really are a great starting place, 20 plus percent of the general population in North America is thought to be diagnosed with irritable bowel syndrome or have symptoms of it and 4 to 5 percent of those patients will have, actually have celiac disease, and those symptoms of irritable bowel syndrome will go away once you treat the celiac disease. So that's actually made it into the most recent American College of Gastroenterology guidelines for diagnosis of irritable bowel syndrome is celiac disease testing.

And I know pharmacists see a lot of these patients, as well, coming in for various gastrointestinal symptomatic medications and recommending that celiac testing be done for those patients would be perfectly appropriate.

The other end of the spectrum would be people who have celiac disease but haven't had any follow-up in a long time, we really like to see people's serologies decrease to normal after they've been on the diet for a year or more, and we'll recheck celiac disease serology. So if that hasn't been done, having a finger stick test done or having some sort of celiac testing done to make sure that their antibody tests have normalized, and if they haven't suggest to them that maybe something's going wrong, maybe there's gluten getting in or something else that they really need evaluation for, those would really be great services to the celiac population.

Tricia Ryan: That sounds great. Now, as we're winding down towards the hour, we're at 3:45, I just wanted to ask you a couple of the questions that came in, and then maybe I'll unmute the line and one was so how long does it take for the villi to heal, and how will I know when I'm getting all the nutrients from the foods I'm eating?

Dr. Leffler: Sure, so the amount of time it takes the villi to heal is very variable. This is, the human body responds in different ways at different ages, and just like any other injury, children heal very well, and it's all, especially those who are older with co-morbidities take a lot longer. So again, generally for children and adolescents, they'll be completely normal within months, whereas in adults, it's sort of you get about a third of people healed completely every two, two and a half years, give or take. So at two years, a third of the people will be normal, at five years, two thirds

of the people will be normal. So it does take a long time for especially older adults with co-morbidities to heal.

In terms of knowing whether you're getting all the nutrients, that's a hard question. A lot of times, you just don't. You have to go somewhat on symptoms. We will test a broad nutritional panel on all our celiac patients, the folate, B12, zinc, vitamin D, iron levels; they're sort of standard for everyone. And in general, if you can, of you see that those are okay, then you can be fairly comfortable that you're doing okay with the other vitamins.

Although, if you have odd symptoms, there will be neuropathy, you can check vitamin B6, there's a lot of other vitamins out there, so it's a combination of knowing really what symptoms people are having and what nutritional abnormalities are associated with those symptoms, and also just keeping an eye on those sentinel vitamins that are often the first ones to be low in patients with significant nutritional abnormalities.

Tricia Ryan: Good. How about, then, the comparative sensitivity of the Biocard Celiac Test compared to other blood markers for celiac?

Dr. Leffler: Yeah, so the Biocard, right now in its current generation, is TTG, tissue transglutaminase based. So in general, it seems to be very similar to a normal TTG as done in the blood test. And that's really sort of our staple blood test for celiac disease these days. So it seems that it still hangs in that 95 percent accuracy range, the same as all our other blood tests.

So one of the things that I would note, and I think this is coming along in the next generation of Biocard, it may actually even be out, is a total IGA level. So one of the reasons that people can have a false negative TTG is if they have IGA deficiency, IGA deficiency is a fairly common and often totally asymptomatic immune deficiency in the general population. It's actually enriched in people with celiac disease. So any time we're suspicious of celiac disease and we get a negative TTG, a total IGA level is one of the first things we'll look at.

Tricia Ryan: So Dan, what percentage of people with celiac disease do not produce the IGA antibodies and will test negative on the standard

blood screening tests?

Dr. Leffler: It's probably about 2 percent, so again, the rate of IGA deficiency in the general population is about 1 in 500, and in patients with celiac disease it's about 1 in 50. So again, it's an uncommon issue. But it is one of the things that makes up that 5 percent false negative rate for any celiac blood test.

Tricia Ryan: And then is there, in the future, something coming, it's like we've had Lactaid for lactose intolerance and things like that, is there a magic pill coming for celiac disease?

Dr. Leffler: I don't think there's going to be a magic pill any time soon, but I think there's some very interesting work on new medications to be adjunctive to the gluten free diet. Everyone wants the pill, and I don't mean that everyone wants the pill so they don't have to do the gluten free diet at all. In most cases, they're perfectly happy to do a gluten free diet within reason. What people don't want is they don't want to have to worry about cross-contamination, invisible gluten, whether something was put on the same fry pan in the kitchen as something else. They want those little bits of gluten to be taken care of.

And that, in itself, would really help out; it would take so much of the burden away. And there's a number of medications now being researched in phase two trials to help with this degree of gluten exposure. There's medication from a company called Alba Pharmaceuticals that tightens up the tight junction between the intestinal villi cells to not let gluten in and there's another medication from a company called Alvine Pharmaceuticals that is an enzyme to break down gluten in your stomach before it can get into your intestines and cause problems.

And I think we don't have the data yet to see if either of these will be successful, but I do think there's a lot of interest in this area now, and I'm hopeful within the next coming years we'll have some good data to say that one of these is actually working and will be on the road to approval. I think it's really going to change the face of celiac disease once we have something more to offer people.

Tricia Ryan: Well, it sounds very exciting. Now, we did have hundreds of questions that we have tried to cover very quickly in 40, 50 minutes, but we will be answering the questions, we'll post this teleseminar on our website. For anyone that's registered, they will get it by email, along with the transcripts, but it will be on the glutenpro.com site, it will be on the pharmacy business website. If people have further questions, they can reach us at info@pharmacybusiness.com, that's info@pharmacybusiness.com.

I do want to thank our sponsors and in particular Dan. It's been great chatting with you, and when I unmute the line, some people may hang up and not stay on the line, but others may have a couple of questions. We can answer a few more questions and take us to the hour. But Dan, this has been fabulous, I always learn when I do this and it's always fun to go back and reread all my notes and become more familiar with this disease as it evolves and all the interesting things that are happening. So again, as well to our guests and their contribution to the questions, it's been great.