June 2009 Issue | Christine Doherty, ND & Alice Bast Executive Director

http://jeffreybland.com/knowledgebase/june-2009-issue-alice-bast-executive-director/

DOWNLOAD AUDIO |DOWNLOAD SUMMARY NOTES |

Welcome to the June 2009 issue of *Functional Medicine Update*. You are going to really enjoy this issue, I can tell you. This will be the first time in the history of *Functional Medicine Update* that we will have a two-part series on a topic. Why will we donate that much time in June and July to one topic? It is because of the importance of understanding gluten and gluten sensitivity. The clinicians of the month that you are going to hear from are two of the leading proponents and experts in the area of gluten and celiac disease. This month we'll set the clinical stage for what, in next month's issue (the July 2009 issue), will be a very new look (at a mechanistic level) at the physiology and pathophysiology of gluten and its relationship to not only regional gastrointestinal problems, but also to systemic relationships. This will really be a very interesting two-part series, I think, to look at the functional medicine nature of gluten as a problem family of molecules related to a triggering of immunological inflammatory response.

As we get into this topic, which will be immunologically focused over the next two months, I thought it might be worthwhile to go back and look at few of the issues that have been recurring themes in functional medicine over the years. I think these issues are important in setting the stage for the discussions in June and July. The first thing I would like to talk about relates to omega-3 fatty acids and their relationship to immune function.

There are certain kinds of (what we call) fundamental nutritional products that have entered the domain of practitioners across a wide range of backgrounds, degrees, and certifications. In the early 1980s, I had the privilege of working with the original group that was bringing softgel omega-3 fatty acid capsules from England to the United States. The original work on omega-3 fatty acids was done by Dr. Hugh Sinclair, as well as by Bang and Dyerberg in Denmark, who had discovered that in the Greenland Eskimos, consumption of very high omega-3-containing diets led to a very significant reduction of incidence of cardiovascular disease. That flew in the face of traditional logic at that time, which said that fat was bad and we should cut fat out of the diet. We were into the anti-fat movement back then and did not differentiate the types of fat.

In Greenland, people were consuming in excess of 70{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} of their calories as fat and yet they had a very low incidence of cardiovascular disease. Researchers originally thought, "Well, they must be genetically protected against this high-fat diet, these Greenland Eskimos." But yet, when they looked at it epidemiologically, it was found that when Eskimos moved from Greenland to Northeast Canada, where they were eating a lower-fat diet (but now in more the Canadian form of fat diet which is the North American fat), that their cardiovascular disease suddenly went up and became like that of other

residents in Canada. Then it was said, "Well hold on, it can't be genetic protection because they've just lowered their fat, yet their cardiovascular incidence has gone up, so there must be more to this."

The work of Bang, Dyerberg, and Sinclair is an extraordinary detective story. They eventually elucidated the active principle within the oil that the Eskimos were consuming through local water mammals in Greenland, which was the omega-3 fatty acids, and in particular, rich eicosapentaenoic acid, the 20 carbon atom fatty acid omega-3 (meaning the last degree of unsaturation and the fatty acid side chain was 3 carbons in from the methyl end of the chain). As an eicosapenta it is 5 degrees of unsaturation and is an oil that is metabolized differently than arachidonic acid, which is a 4 unsaturated fatty acid up to 20 carbon in length, in which the last double-bond is 6 carbons in from the methyl end. The arachidonic acid family has a very different downstream elaboration into prostaglandins (the 2 series prostaglandins), which are proinflammatory, pro-platelet adhesive, and pro-cell proliferative versus the omega-3 fatty acids, which move downstream into a different series of eicosanoids that are anti-inflammatory in nature and balance the activity of the arachidonic acid-derived prostanoids.

Then: Only Forward-Thinkers Seemed to Understand the Role of Omega-3 Fatty Acids in Cardiovascular, Mental, and Immunological Health

In the 1970s, a group in New York state and New England-the Ames group-included forward-looking practitioners (medical doctors) that met with people like Donald Rudin and David Horrobin, who, early on, were talking about omega-3 fatty acids and health in the United States. At that time, David Horrobin was based in Canada (in Montreal) as a medical school professor working on psychiatric health. Don Rudin was a psychiatrist in the northeastern United States. They both did a brilliant job in communicating with the medical community in the Ames group about the role omega-3 fatty acids play across a wide range of physiological functions--not just cardiovascular health, but mental health and immunological health.

The first supplements that came to the United States that contained omega-3 fatty acids were called MaxEPA, produced by the RP Shearer Company in England. I was fortunate to be one of the spokespeople for this new omega-3 fatty acid preparation, and was actually able to get funding (as a university professor) for studies on MaxEPA incorporation into red cell membrane lipids in human student volunteers (medical student volunteers). I published some papers back in the early 1980s on this topic, and was one of the first investigators looking at the role of MaxEPA and incorporation with supplemented diets of people living in the states.

Validation Comes in a *New England Journal of Medicine* Article

Later, in the middle to late 1980s, Elias Corey and a group of collaborators at Harvard University published what I think is a landmark paper in *The New England Journal of Medicine* describing the effects that omega-3 MaxEPA supplementation had in human volunteers on monocyte adhesion, chemoattraction, and ultimately leukotriene secretion as it relates to pro-inflammatory mediation in people supplemented with omega-3 fatty acids.[1] Once it was in *The New England Journal of Medicine* it was on the big board; many people hadn't understood why oils would have any effect on the immune system when this paper was published. For those individuals who were already in the flow of understanding, it was a very big breakthrough to have a paper published showing that human volunteers supplemented with six grams a day of a mixture of different omega-3 fatty acids and omega-6 polyunsaturated fatty acids (MaxEPA) had a marked clinical effect on their stimulated production of leukotrienes as it relates to downregulation of 5-hypoxygenase enzyme activity. This article was a big

"wow," and it indicated that there might be something to the story that omega-3 fatty acids can have an anti-inflammatory or an inflammation-modulating effect.

Now: Many Papers Looking at Mechanisms and Clinical Activity

From that period on (from the publication of *The New England Journal of Medicine* paper until now, 2009), we have seen literally thousands of papers published in many, many journals looking at mechanisms and clinical activity. I am specifically thinking of the work of Joel Kremer at Albany Medical College in New York showing that in patients with rheumatoid arthritis, supplementation versus a placebo led to improved joint mobility, lowered pain, lower involuntary use of pain medication; this was work that was published in the late 1980s and early 1990s.[2,3] As this concept has rolled forward, I have heard of studies showing that people with inflammatory bowel disease taking an enterically coated EPA formula had lowered inflammation and better recovery from inflammatory bowel disease. We've seen many, many different modifications and extensions since the early observations of Bang, Dyerberg, and Hugh Sinclair in Greenland with the Eskimos. In an issue of *Functional Medicine Update* several years ago, I was very fortunate to have the opportunity to interview Dr. Dyerberg, who gave a brilliant historical record of these discoveries and his work in Greenland and how those observations advanced this whole field.

What Sources of Omega-3 Supplements Are Available Today?

With that in mind then, what are the various sources of omega-3 fatty acid supplements that are now available today? The story has gotten a little bit more complex. We know that the first member of the omega-3 fatty acid family is a substance called gamma linolenic acid, which is an 18-carbon atom fatty acid that is omega-3 with 3 degrees of unsaturation. Through a series of elongase and desaturase enzymes, gamma linolenic acid becomes eicosapentaenoic acid (or EPA) (that's a 20-carbon fatty acid with 5 degrees of unsaturation). Ultimately that goes into another chain elongation/desaturation to become docosahexaenoic acid (or DHA). So we have this kind of metabolic tree, so to speak, of the omega-3 fatty acids that most people in this field have memorized and recite on demand; it's kind of a right of passage to know this fatty acid biosynthetic pathway.

The sources of omega-3 fatty acids that are available now include both vegetable sources and animal sources, and there is some confusion in the marketplace as to what are the most efficacious and clinically beneficial forms of omega-3 supplements. Let's just review this very quickly. As a reminder, the omega-3 metabolic biosynthetic pathway starts upstream with an 18-carbon fatty acid called alpha linolenic acid (or ALA). This is a triply unsaturated omega-3 fatty acid that is then desaturated and elongated by enzymes into the 20-carbon atom fatty acid with 5 double bonds omega-3 called EPA (eicosapentaenoic acid), which is then further converted by elongation/desaturation into the 22 carbon atom fatty acid with 6 double bonds called docosahexaenoic acid (or DHA). It has been thought that one could derive the benefit by going upstream and utilizing the vegetable origin of the downstream animal DHA and EPA by using ALA, which is derived from things like cold water vegetable oils such as borage oil or flax seed oil. It has been recognized that there is benefit from supplementation with these ALA-containing oils One can use data from studies like the Lyon Heart Study, which showed that individuals who consumed diets that were higher in calorie percent of the omega-3 vegetable oil ALAs had a lowered incidence of cardiovascular disease. This was one of the most remarkable clinical intervention trials in nutrition that has ever been published. In fact, the results were so dramatically different between the group that took the omega-3 oils in their diet (polyunsaturated oils) versus those that ate longer-chain saturated fatty acids, that they had to call off the study because there was such a significant increased risk in incidence of

cardiovascular in those individuals who consumed the longer-chain saturated fatty acids. There seems to be something very cardioprotective about the polyunsaturated omega-3 oils.

We recognize that these fatty acids are very labile to cooking and to oxygen (to high temperature and oxygen), and also to light. These need to be freshly prepared and kept cold, and ideally kept under an inert atmosphere if they are going to be stored for any period of time. Some EPA is found in some vegetable sources but at a very small level. We would normally think of EPA as being more animal-derived origin (fish, in this case). Fish don't make EPA from scratch; they basically eat the precursors from the krill and the krill gets it from the phytoplankton, so it comes up through the food chain in a biosynthetic pathway. So the ALA gets converted to the EPA, which the fish eat and then there is some conversion into DHA.

We might say, "Well, let's go back to the source-to the vegetable source," and certainly there is some advantage in consuming the omega-3 vegetable oils, however the conversion in humans (the enzymes that are required to do the elongation and desaturation of ALA into EPA) is very slow in process and it is difficult to elevate EPA levels by giving ALA supplementation. If you really wanted to have a marked effect on EPA levels within membrane phospholipids, it is better to give EPA directly.

The other vegetable source is DHA because there are algal forms of DHA. DHA has now become a major supplement that is fortified within infant formula. An algal-derived DHA product that can ultimately increase the omega-3 content of infant formula has been identified in clinical trials to be very effective in improving retinal function and potentially brain function as well (two percent of the phospholipids of the brain are occupied by omega-3 DHA). It has a very important functional characteristic, and it is kind of a conditionally essential nutrient. As such, it must be obtained through the diet. For infants and pregnant women, proper omega-3 fatty acid intake is very important, including DHA directly. One can get an algal or vegetable-based omega-3 chain elongated desaturated product directly from vegetable-based products. If you want EPA in high concentration, however, you really have to go to an animal-derived product (at this point, fish) to really create the highest concentration (to get up in the 60{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36}, 70{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} range).

It really depends on what the clinician is trying to do. In general nutrition intake (for salad oils and so forth), the ALA flax seed oil or sesame oil can be very desirable, but for cooking at high temperature one probably wouldn't want to use the very labile omega-3-rich vegetable oils because they are very easily damaged by heat and oxygen. You probably want to stay with the monounsaturated linoleic acid (olive oil) for those purposes. If you are trying to improve neuronal composition and retinal composition, the DHA-rich oils and even vegetable-based DHA can be very primary and therapeutic in that area. And if you are looking for the anti-inflammatory effects then you're probably going to be looking at the EPA-rich oils that come from animal products (from fish). Again, the therapeutic dose of these oils for anti-inflammation or immune modulation is somewhere between, say, one and three grams per day of omega-3 EPA. So if you have a product that is something like 60{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} EPA/DHA, then you are going to have to have three one-gram pills a day to get to your threshold of around a gram of EPA (just to give you kind of a sense as to magnitude). That would be about three grams of the mixture of EPA/DHA high potency formula. I hope that helps to make some sense of this interesting immune modulation question related to the omega-3 oils.

The other companion topic that I think will help lead into our discussion this month with the clinicians has to do with insulin resistance/hyperinsulinemia/inflammation, and the relationship that has to immunological balance and how that relates to things like omega-3 oils and other immune-modulating nutrients. In the functional medicine model, our approach is to look at the antecedents that are related to events that trigger the release of various mediators that modulate function and ultimately produce the signs and symptoms of different duration, frequency, and intensity in the individual. It is a different model of evaluating the patient than focusing on a differential diagnosis. It doesn't mean that the diagnosis of a disease is irrelevant, but what we are looking for is the underlying kind of ecology of what we later call a disease by looking at antecedents, triggers, and mediators giving rise to signs and symptoms. This information is then focused through the lens that we call the functional medicine matrix, which gives rise to an understanding (hopefully) of the systems biology consequences of disturbances that give rise to signs and symptoms

With that in mind, let me talk about some very interesting work that is emerging about cognitive performance-related issues (dementia) and various types of antibodies that are formed as a consequence to response to inflammatory mediators.[4] One of the major triggering devices for these inflammatory mediators appears to be that of events that lead to the production of advanced glycosylation end products (or AGEs-AGE proteins). These proteins upregulate the activity of what are called the receptors of advanced glycosylated end products (the so-called RAGE receptors) on the surface of white cells. Basically, when a person is insulin resistant and having inflammatory mediation they are "enRAGEd" (to use kind of a play on words). If it occurs in the microglia of the brain, this can have effects on neuronal function leading to neuronal apoptosis and cell death, and ultimately to decline in neuronal reserve, which we later call cognitive dysfunction.

This dementia/cognitive performance connection is very, very strong. In the next discussion we're going to be talking about what could trigger these RAGE receptor activations and immunoglobulins that relate against brain function (myelin as well as neuronal function). Are there other agents (like sporing proteins) that may trigger this in immunologically susceptible individuals? Of course the answer is yes. Gluten is going to be the agent we'll be discussing. Let's turn to our wonderful discussion with our two clinicians of the month this month.

The first interview is going to be with Alice Bast. I want to make sure to say that the opinions Alice will be sharing with you are her own personal opinions, not necessarily that of every member of her scientific advisory group for her foundation, or the foundation itself. She is an individual who has extensive personal experience with this gluten-related story.

INTERVIEW TRANSCRIPT

Christine Doherty, ND
Balance Point Natural Medicine
354 Nashua Street
Milford, NH 03055
www.pointnatural.com
www.glutenfreevitamins.com

Of all the people I have met, Dr. Christine Doherty has certainly focused her practice very effectively on

intervention with patients who have complex immunological problems that are associated with gluten and alpha gliadin sensitivity. Let me quickly introduce Dr. Doherty's background. I am very proud to say she is a graduate of Bastyr University, and received her degree from the naturopathic doctorate program in 1998. She has been in private practice in New Hampshire since 1999 and has worked with thousands of patients, all ages, with different forms of chronic illness. In 1999, Dr. Doherty was appointed by Governor Shaheen of New Hampshire to a three-year term on the New Hampshire Osteoporosis Council. She was Vice President of the New Hampshire Association of Naturopathic Doctors from 2002-2005. She attended the National Institutes of Health Consensus Conference on Celiac Disease in 2004 and has been a medical advisor and speaker for the Southern New Hampshire Gluten Intolerance Association since 2004. Recently (in 2008), Governor Lynch appointed Dr. Doherty to the New Hampshire Board of Naturopathic Examiners for a five-year term. She has a very esteemed background and a clinical series of experiences. Dr. Doherty, welcome to Functional Medicine Update, and it is really a privilege to have you as a representative of the naturopathic community.

CD: Thank you so much, Dr. Bland. I feel truly privileged to be with you today.

JB: Let me start with a question that I like to use to initiate these conversations: Can you tell us a little bit about how you made the decision to become a naturopathic doctor? I know that you traveled through your undergraduate education at Concordia University in Montreal, Quebec, so you probably have some French in your background. Maybe you can tell us how you got to Bastyr.

Personal Experience with Celiac Disease Leads to Medical Degree

CD: It was really through my own illness, I think. My undergraduate degree was actually in fine art; I majored in painting and art history, and the last thing on my mind was that I would ever go into medicine. But I was really interested in alternative medicine, and I spent a summer working at an art gallery in Santa Fe, where I met an 80-year-old chiropractor, Jay Shearer, and he really sort of revolutionized my way of looking at my health. He told me I had to go off dairy and he modified my diet more. I'd been working to modify my diet since I was probably about 13 because I had been sick most of my life (since childhood), and I had a sense that something food-related was the problem. I'd gone through being macrobiotic, I'd gone through being vegetarian, vegan, you name it. He really helped me feel better, and that really opened my eyes to the concept of actually having a career in natural medicine. At that same point in time, a friend of mine had started dating a first-year student at Bastyr in the naturopathic medicine program (from Montreal). I had never heard of naturopathic medicine, and we sat down for lunch and by the end of that lunch I thought, "This is what I am going to do with my life." I went back to school and I got a pre-med degree (because, obviously, the fine art degree wasn't going to cut it), and I never really looked back.

As I said, I had been sick for a long time and I'd been to a lot of different doctors over the years and no one could ever make sense of my seemingly unrelated symptoms and my chronic anemia. I'm blue-eyed and blonde. I used to bruise really easily. I actually had one doctor diagnose me as a blue-eyed blonde and that that was the cause of all my problems, which I knew was just a ridiculous answer. My illness was part of what drove me to get my doctorate in medicine. The MDs, at that point, didn't have the answer I was seeking, so that's where naturopathic medicine made sense to me.

JB: You've done such a magnificent job of taking that experience and translating it into help for literally thousands of patients. I think the interesting part of all of our journeys is what we collect as experiences

(either our own personal experiences, or that with loved ones, or family, or friends, or in the world at large), and we then become our stories, basically, and our stories become our life and they kind of guide us toward our trajectory. Can you share a little bit about this path? It sounds like you had some very extraordinary epiphanies that kind of guided you, probably, as to how to better help your patients.

CD: Yes. I made it all the way through naturopathic school and I still didn't really know what was wrong with me. I still didn't feel like I had the answer I was seeking. To give you more background on my medical history, when I was young, even as a child I remember having joint pain, bone pain, abdominal pain, irritable bowel syndrome. It got to the point where I just stopped telling doctors about what symptoms I was having because I knew they couldn't really make sense of it. As I got to my teen years, I started getting really heavy periods and weight gain. The bone pain got even worse, and I remember telling my dentist that whenever I drank beer my gums would bleed uncontrollably. He said, "There is absolutely no connection between beer drinking and gum bleeding. You just need to floss your teeth." I remember thinking, "If I floss my teeth I'm going to bleed to death." It was definitely a connection in my mind.

When I was about 13, I developed a really itchy, vesicular rash on my lower back, which would travel around over the next 25 years. I spent one summer in France, living on baguettes, and by the end of that summer I had this rash all over me. When I got back to Canada and went back to my regular diet, the rash went back down to one or two spots. In retrospect, I now know it was the dermatitis herpetaformis.

As I mentioned, I experimented with a lot of different dietary pathways. By the time I got to Bastyr, I started getting even sicker. My liver became inflamed (my liver enzymes were elevated). I was always anemic; my iron levels (my ferritins) would be around 6 or 7 on average. I had a lot of infections. I was definitely irritable, moody, and fatigued a lot.

It all started getting much more serious after I got married. I married an acupuncturist right after we graduated and we started trying to get pregnant. Two years later I still wasn't pregnant, so that was when we started to think, "Okay, I'm definitely medically infertile at this point." My husband and I undertook a really intensive program. We took gluten out of our diet (we both did it). We did yoga everyday. Lo' and behold, I got pregnant the first month. In retrospect, that was the major piece of the puzzle. I wish I had known that gluten was really the cornerstone of everything, because I went right back to eating gluten as soon as I was pregnant. I had a very complicated pregnancy. It was unbelievable, really. I developed hypertension. I got gestational diabetes. Something bizarre happened to my thyroid; it was both hyper and hypo. I even wound up at an endocrinologist's office and they couldn't make heads or tails of it.

I went into premature labor at 27 weeks. With the acupuncture everyday I managed to keep the baby to term (I went on bed rest). The delivery was complicated. I developed septicemia, so I was very ill. I had the baby and that all went fine, thank goodness. About four days later I developed severe abdominal pain; I mean, just mind-boggling pain. I wound up going back to the doctor and he said, "Oh well, you've just got a urinary tract infection." I had done an abdominal exam on myself and I found a huge abdominal mass. It turns out it was a fibroid (a necrotic fibroid), but they thought it was a sarcoma, which basically-I knew-would have meant that I probably only had a year to live. Initially they thought it was a hematoma, so they watched it.

Eight weeks later (bear in mind I have a newborn through all of this), I had a radical cancer surgery, and

they basically took out half of my small intestine, ten lymph nodes, two-thirds of my large intestine, and it was quite a rough recovery. And then I basically went into immune failure for the next two years. I got the Norwalk virus. I got trigeminal neuritis. I got four bouts of bacterial pneumonia.

Eighteen months later, I was back in for more surgery from obstructions from adhesions and they removed my gall bladder. I definitely felt like I was dying. I knew there was something wrong with me, and I just couldn't figure out what it was. No matter how much iron I took my iron levels wouldn't come up. I was getting pretty desperate to find the answer. A low point was when I developed severe nystagmus. I was vomiting uncontrollably at a play date at the local park and had to be carried out by ambulance. I had severe bouts of vertigo for about another year-and-a-half after that happened, so I was definitely having neurological problems. I haven't even emphasized the gut piece, but I was having constant gut pain.

One day I was sitting in my clinic waiting room and I was reading the magazines on the coffee table. I think Eat Well was the magazine, and it had a headline that said "Could Wheat Be the Problem?" (or gluten-I can't remember the exact title). "Do have constant anemia? Do you have infertility?" It kind of listed through a lot of my symptoms, and it was the epiphany that I had been waiting for. I tested myself, and sure enough it came up positive. I went gluten-free, and I was really lucky that I responded. The rash went away (finally!). All my gut symptoms healed up. My immune system is much, much better. I occasionally get a cold-once a year, maybe (my doctors had told me they had surgically immune-compromised me because they had removed so much of my gut). I have no doubt the gluten-free diet saved my life. I feel really blessed, and I guess evangelical, since it was my past that led me to this point. That is kind of the synopsis.

JB: First of all, thank you very much for sharing that. I know that's a very, very personal story and it probably brings back all sorts of memories. For people listening, it certainly, without any question, is a resume of qualification of your expertise in this area, that's for sure...

CD: Come by the hard way...!

JB: No kidding! I have been fortunate to hear this story before because you and I spoke and I was deeply moved and very touched by not only your vigilance as to how you walked through this personally, but by the maintenance of your positive attitude, which undoubtedly was a factor in your recovery because not everybody has that resilience, emotionally. I'm reminded of the book, which I have cited in past issues of Functional Medicine Update, called How Doctor's Think, by Jerome Groopman from Harvard.5 He starts that book by going through a case history--a medical detective story that goes on for many pages--about this poor woman who has all these symptoms, and all these problems, and multiple surgeries, and the conclusion of the story is the same as your conclusion.

Length of Time to Diagnosis Can Lead to Trauma
CD: Oh yes. I'm not alone. I have met a lot of other patients with fairly similar histories. The average length to diagnosis is 9 years, and there are a lot of people out there for whom it is 25 years. You accumulate a lot of trauma (medical issues) in that 25 years.

JB: Could tell us a little bit about some of your clinical high points since you've had this extraordinary learning experience yourself? I think for most people they still think that food has to be a friend, and that

wheat within our food is considered a good food group. How can we suddenly be saying there is something bad about it? Maybe you can tell us a little bit about, in your clinical work, how you present this to patients and some of the things you have seen in patients as they have made their own changes and transformations.

Celiac Disease Can Lead to Long-Term Nutritional Deficiencies
CD: I totally see what you are saying about how we think it is a health food. I remember when I was first diagnosed, I'd think, "What do you mean I can't have a piece of Ezekial bread but I can drink a Coke?" It turned my whole concept of what was good and what was bad on ear. Obviously a Coke would not be good, but suddenly that was something that wouldn't kill me, whereas a piece of bread would, and that was just a really bizarre paradigm shift.

In terms of the clinical approach to patients, it's going to sound almost embarrassingly simple. What I have found, over the years, is that you have to start with the nutrition. When I was at the NIH Consensus Conference there was a moment that was another epiphany for me and has really guided my work. A woman, Cynthia Cooper, who is the head of the Gluten Intolerance Group of North America, said the statistic that 10 years after diagnosis 50 percent of celiacs still have multiple nutritional deficiencies. I have definitely seen that in practice. People have been gluten-free for years, but they are still not feeling well. They are tired, they are irritable, they are depressed, they are not sleeping well, they have brain fog, and they may still have gut symptoms.

This is where I really see starting with the basics of nutritional supplementation. I often see patients who have been to other doctors (including holistic doctors) and they have been given more specific things (for the liver, for example), but often nobody has just looked at the basics, like whether they have an essential fatty acid deficiency. They often have issues with fat soluble vitamin absorption, so it is a really good idea to give them the active forms of all of them, and I give them the fat soluble versions of vitamin A, not just beta carotene, because I find they don't convert the beta carotene very well.

The other sneaky thing about this population is they have been suffering a long time. Just as I got to the point where I didn't bother mentioning so many of my symptoms, I find you have to ask specific questions about things like night vision and how are they sleeping. They'll try to boil it down, but if you start asking about things like chronic canker sores (which is another symptom I definitely had for years), that is when they start seeing they've got all these symptoms of deficiencies, but they're not putting it together with their celiac (and neither are their doctors, in many cases). A lot of those are just symptoms of deficiency. Getting the B vitamins in there, the calcium, the magnesium, all the minerals, the essential fatty acids will often do wonders.

Beyond that, you sometimes have to look for other food intolerances, enzymes, and food allergies. One theory that I'm working on right now and seeing kind of develop in practice is that I think a lot of patients aren't true celiacs in the sense that they have the IgA-antibodies and the villous atrophy, but they have all the same symptoms and they definitely respond to the gluten-free diet. I think a lot of them actually have an IgE-wheat allergy. When I have brought that up with some of the celiac specialists they have said, "Oh, there's no good test for that." There is so much more to the picture than we really understand about gluten, and I don't want to boil it down to just celiac. There are so many things that respond, clinically, to the gluten-free diet. But I think the important thing is to rule out celiac first, because once they go gluten-free it is much more difficult to test them and the serology is negative fairly quickly.

JB: That leads into, I think, a very important question for those who may be less familiar than you in assessing patients. First of all I want to ask a simple question: did you ever have a mucosal biopsy yourself throughout this whole history? Did you have villous atrophy?

CD: Strangely I don't think ever went to a gastroenterologist even though I had so many symptoms. I had a biopsy set up, and at that point it was about a four-month waiting list. I was getting sick about every three weeks, so I knew I would have another bout of pneumonia and probably another couple of nasty infections before I would get there, so I just didn't have the patience. In retrospect I realize there is a lot to be said for getting the biopsy. I obviously never wanted to go back and challenge it because it had such a huge clinical impact on me. For patients, I do emphasize that they will be asked over and over if they have ever had the biopsy. For communication, it's the only way to practically know how much damage is happening internally. So yes, I think there's definitely a place for the biopsy, but I wound up skipping it just for timing reasons (and probably out of desperation, frankly).

JB: How about when you work up a patient? What are the assessments, or testing, or diagnostic methods that you have found useful?

Clinical Methods for Assessing and Testing Patients for Celiac Disease
CD: I usually start with the celiac panel. That would be a tissue transglutaminase IgA, anti-endometrial IgA, total IgA (because about 4{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} of patients are IgA-deficient), and then the anti-gliadin IgG and IgA, and sometimes (especially if they have a family member) I'll do the genetic screening as well (because theoretically if they don't have the gene, they likely won't ever develop celiac). That's what I start with, and then if they come back positive then I would refer them on to a gastroenterologist. Some people absolutely refuse to do the biopsy, in which case I tell them that as long as they make peace with it and understand that it is a definite part of the diagnosis then fine, but I respect their choices. Typically I explain to them why they probably would want it (I find that a lot of people are super excited to have an answer that finally ties together all of their symptoms). They go gluten-free and then they start feeling better, and then they start saying, "Well, I never had the biopsy. Maybe I really don't have to be on this diet for the rest of my life." They swear to me up and down that will never happen, but I've seen it happen time and time again). That is an interesting thing I have learned from experience.

JB: After you've got all this data in on a person and let's say it looks equivocal, which often is the case, what do you do at that point? Do you have to have iron-clad information, or how do you read the shades of gray?

Celiac Testing Data Can Be Clear as Mud
CD: You're so right. I'm sure any clinician who is reading these tests is seeing the shades of gray. Often I'm brought in to try and interpret. I call it "clear as mud." There are a lot of different tests and one can come up positive and not another. But the other really important piece to remember about the diagnosis is the third part, which is the response to the diet. I try to get as much information as I can. I make sure they go to a gastroenterologist who is familiar with the interepithelial lymphocyte screening, so they don't just look for total villous atrophy; they know to do the stains (because that can show early celiac).

Once we have all of the information or we see if they have a family history or if they've got the genes,

then I'll do a trial of the gluten-free diet. I have started testing with the immunocap IgE test for wheat, or I will also do an IgE anti-gliadin and wheat profile, and a lot of times they come up on that. To the best of my knowledge, it doesn't necessarily mean they'll progress to celiac. Again, I often like to have the genes to know how at risk they are for going down that road.

Basically, the reason patients come to see me is they want to feel better. They don't care so much about the testing, it's the doctors that get all caught up in it. They just want to feel better and that's where the gluten-free diet comes in because you don't know until you try. Another really important thing that I've learned over the years that is hard to get your head around as a doctor is that when it comes to the testing, there is almost no correlation between how positive the tests are and how clinically ill the patient is. I have seen people with tissue transglutaminase (let's say normal is over 3) of 500, positive biopsy, and their only symptom is a little acid reflux occasionally. And I have seen other people who are at a 4 tissue transglutaminase, and they are literally dying from multiple autoimmune diseases and they are completely collapsing and in and out of the hospital.

JB: Very, very interesting. Again, we don't want to treat the numbers, we want to treat the patients.

CD: You can't with this disease because the numbers are deceptive. You really don't know, and then with the neurological patients, often they'll respond with the anti-gliadin antibodies and not so much with the tissue transglutaminase. The bottom line is I try to explain all this to patients, which can be a challenge, and then we do a trial of the gluten-free diet. Often they'll see huge response with that, especially in conjunction with, (as I said) basic nutrition. A lot of times their adrenal glands are extremely taxed because they have been through hell and they have been really sick for a long time. Their moods are often an issue. The number one symptom in children is irritability. I have seen a couple of kids now who had been diagnosed as bipolar, and they were celiac. We get them off the gluten and on a multi, some fish oil, and some probiotics. Within two or three months they are completely different personalities.

JB: That is so interesting. I have a quick anecdote for you. In 1978, I was on sabbatical and teaching at the Evergreen State College in Olympia, WA. My class was a very interesting group of students that followed me through the whole year because of the way the curriculum was set up that college. One of them was an older-age student who was the wife of a math professor at the university. She had a son who was nine and had all sorts of neurocognitive problems and behavioral problems. He had been seen by the school psychologist and was going to be in Special Ed, and they were very worried about him; he seemed like a very troubled young boy. Not knowing nearly what you know-this is back in '78-I kind of naively said (based on what I had read), "Maybe he ought to be taken off gluten-containing foods and dairy for a short period of time as kind of an elimination diet just to see how he does." I had been to a previous seminar with the founder of the American Academy of Environmental Medicine, who was a world-expert in food allergy testing by elimination, and so I thought maybe it would help. In three months, that boy-as you are describing-completely turned around. The dark circles under his eyes went away. He gained weight. He gained energy. He was a top student in his class. They had thought he was retarded; he was not retarded. For me, that was a real experience.

CD: It's miraculous, isn't it, when you see that kind of incredible transformation, just by taking one protein out of the diet? There is this wonderful pediatric gastroenterologist at UCLA, and at one of her lectures she said that all of the animals who are adapted to eat gluten have four stomachs and chew their cud. I thought, "You know, our little human digestive tract..." This is part of where I think gluten

intolerance comes in, too. If there is any level of compromise, I think gluten is one of the first things to go. It is a spiral molecule, first of all, and so I think our enzymes just have a hard time getting in there and breaking it down, but I often think of the four-stomachs and chewing cud. This stuff is really hard to digest.

JB: Let me ask you about treatment because I know there is a very big discussion on this point as to how rigorous exclusion of gluten needs to be to get clinical improvement. Maybe there are different variations on a theme, relative to presentation (some people can tolerate more than others). What is your view, clinically, on how rigorous the diet needs to be?

Compliance with a Gluten-Free Diet

CD: In the patients I see (and a lot of people come to see me because they haven't gotten better from the first-line diets alone), it becomes about contamination and environmental issues. I wind up doing a fair amount of troubleshooting, for example, "You can't handle your dog food and then pick up a piece of your gluten-free toast. You are going to get sick." The way I kind of describe it to patients is, "When you got the flu, did you ever see the flu get into your system? That is what our immune system is designed to deal with: things that we never even see. So the molecular amounts of gluten (or, let's say, a crumb of something) is plenty for our immune system to have a full-blown reaction to."

You are absolutely right. Some people are more sensitive than others. The problem with celiac is that you can't rely on the symptoms, so that person may be able to have a burger every once in a while, or not be particularly careful about their soy sauce. They could be marching down the road to cancer, but not necessarily have symptoms. They can truly be asymptomatic. It's weird that you can't monitor how dangerous the disease is and how strict they need to be just based on symptoms, so I tend to err on the side of caution and recommend everybody be as strict as they can. Have the separate toasters. Don't use the wooden chopping blocks where people cut the bread in the family. Don't use sponges that then spread the gluten all over the counter and then you put down your piece of bread or your spoon. I see a lot of patients get better once they get that rigorous about it. It really comes down to the molecular level, I think.

JB: And how about compliance? Often people will express good intentions, but when it comes to the rigors of daily living, stuff is lost in translation.

CD: I'm sure that happens all the time. Where you can really see it is the recommendation that if one person in the family is diagnosed with celiac, every other member should be tested. (Every first-degree relative is supposed to be screened, symptomatic or not.) With all of the patients I have worked with, I have seen maybe one family where they all agreed to get tested. Usually they say, "I see how you're living and I don't want to do that. I don't want to know." There are a whole lot of people out there who literally have celiac and absolutely refuse to be tested because they don't want to comply with the diet in any way, shape, or form, so yes, it is a spectrum. I think a lot of the people who see me are pretty motivated because they are fairly sick. I find my patients (as far as I know, anyway-they don't always tell me) are pretty compliant, mostly because they feel better. With any disease (and I know you certainly know this), it isn't just about the diet. People have to be exercising, they have to be sleeping, they've got to be well-hydrated, and they've got to be happy. They have to have beneficial emotional pieces in their life. I work on it beyond just the diet; you really have to look at the whole thing.

JB: I think that comes across so strongly, just hearing your tone of voice, your affect, and the way that you approach this. I think, again, it comes down to the art of health care that has to do with the patient/practitioner interaction-that very privileged moment in the exam room when you are talking with them and you are presenting something that is different. I get the feeling I'd love to be on the diet with you as my counselor.

CD: Thank you!

JB: Let me close with one last question. As you have had this ever-increasing experience of watching patients get better through this approach, what do you see the future looking like? How do you see the trajectory taking us into the future?

CD: I'd like to think that all the undiagnosed celiacs are finally going to get discovered (minus the ones who refuse to be tested, of course). I read a statistic yesterday that said more people in America have celiac disease than ulcerative colitis, Crohn's disease, and cystic fibrosis combined.6 I thought that kind of drove the point home. What I'm hoping-and I think everybody who is advocating for celiac is hoping-is that really the big thing is to get people diagnosed. There's a ton of great dietary resources out there. There are a ton of restaurants that now have gluten-free menus, lots of national chains. It's a huge, exploding market in terms of the options; it has never been as easy to be gluten-free as it is now and I'm sure it's just going to get easier. I'm optimistic. I've seen a huge change just in the five years that I've been gluten-free. When I lecture to doctors, it's still about, "Here are the celiacs; recognize them, screen them, and then get them on the road to wellness." But once they are gluten-free and their deficiencies are fixed, they are just like everybody else. Their mortality rate is just like everybody else. We can be fine.

JB: You are an incredible model for that-your spirit, your energy, your advocacy, you are going to be a guide for many, many thousands of people, both those that are in your practice and those that are touched by the people that have been in your practice. Thank you very, very much. This has been extraordinarily insightful. Anyone who may have come in to listening to this that didn't have some sense as to the depth of this issue certainly couldn't go away without now seeing the impact of it and the importance of it. Dr. Doherty, thank you so much. Our very best to you and keep doing what you are doing so well.

CD: Thank you and same to you.

I hope you got as much out of that extraordinary two-part interview with Alice Bast and Dr. Christine Doherty as I did. That was a tremendous amount of news-to-use and dense both in personal experience as well as general information on the whole gluten effect. Of course, we're going to be hearing much more about this, mechanistically with our discussion next month in the July issue.

A New Book Called The Gluten Effect

I did want to give you some information about a good book that you can send your patients to. It is a contemporary book on the gluten story that is called *The Gluten Effect*.[7] The authors are two dear friends and colleagues-the Petersens (Dr. Vikki and Rick Petersen). This book is now available in most bookstores, or from Amazon, or any of the book sellers-*The Gluten Effect*. It is written for the patient, to bring them up to speed as to the implications of the story beyond that which they might have heard of frank celiac disease. The book is another resource that you might keep in mind for your patients-*The*

Gluten Effect.

Bibliography

1 Lee TH, Hoover RL, Williams JD, Sperling RI, et al. Effect of dietary enrichment with eicosapentaenoic and docosahexaenoic acids on in vitro neutrophil and monocyte leukotriene generation and neutrophil function. *N Engl J Med*. 1985;312(19):1217-1224.

2 Kremer JM, Jubiz W, Michalek A, Rynes RI, Bartholomew LE, et al.

Fish-oil fatty acid supplementation in active rheumatoid arthritis. A double-blinded, controlled, crossover study. *Ann Intern Med*. 1987;106(4):497-503.

3 Kremer JM, Lawrence DA, Jubiz W, DiGiacomo R, Rynes R, et al. Dietary fish oil and olive oil supplementation in patients with rheumatoid arthritis. Clinical and immunological effects. *Arthritis Rheum*. 1990;33(6):810-820.

4 Wilson JS, Mruthinti S, Buccafusco JJ, Schade RF, Mitchell MB, et al. Anti-RAGE and Aβ immunoglobulin levels are related to dementia level and cognitive performance. *J Gerontol A Biol Sci Med Sci*. 2009;64A(2):264-271.

5 Groopman, Jerome. *How Doctors Think*. Boston: Houghton-Mifflin Company, 2007.

6 http://celiac-disease.com/facts-statistics-about-celiac-disease/

7 Petersen, Vikki, and Richard Petersen. *The Gluten Effect*. True Health Publishing, 2009.p>