

CELIAC DISEASE: **Sometimes Silent, Often Misleading, ALWAYS SERIOUS**

An estimated 1 in 20 individuals with type 1 diabetes have celiac disease, a gluten-sensitive disorder. Many more are harboring its markers and most don't know it. Widespread screening could prevent serious health consequences.



By Jo Cavallo

Until last year, Renee Bennett thought the chronic stomachaches, fatigue, and depression her daughter Melissa had been suffering from for years were related to blood sugar highs and lows. She says she still “kicks” herself for not suspecting that something else—something beyond type 1 diabetes—was causing the problems.

Melissa, now 21, was diagnosed with type 1 diabetes when she was 9. She says she remembers having gastrointestinal problems and bouts of fatigue from the start. “I had stomachaches after eating, but they would come and go and they weren’t so severe, so I thought that was normal. Coping with diabetes you learn to have a higher tolerance for pain,” she says. “I did have extreme fatigue but that was always something I attributed to other things like depression and being on antidepressants.”

Neither mother nor daughter considered celiac disease a possible culprit. “It’s the classic misunderstanding that when you picture someone with celiac disease you picture a child with a big extended belly, skinny arms and legs, stunted growth, and constant diarrhea,” says Renee Bennett, who is a JDRF volunteer and member of JDRF’s Lay Review Committee. “Melissa is 5’4” and has never had growth problems.”

Last fall, a friend and fellow JDRF volunteer told Bennett that her 11-year-old son’s endocrinologist had begun routinely screening patients with type 1 diabetes for celiac disease and that her son had tested positive for it. “When I heard this, I thought I should have Melissa screened, too.”

Melissa was tested for and diagnosed with celiac disease in October 2003.

MORE COMMON THAN MOST PEOPLE THINK

Gluten-sensitive enteropathy, commonly called celiac disease (CD), is a chronic intestinal disorder caused by a hypersensitivity to gluten proteins found in wheat, rye, barley, and possibly oat products. Normally, ingesting such proteins does not cause an immune response, but in patients with celiac disease the immune system is abnormally activated by gluten, triggering an inflammation

CELIAC DISEASE





CELIAC SYMPTOMS: WHAT TO LOOK FOR

Classic symptoms of celiac disease include chronic diarrhea or constipation, abdominal pain, gas, and bloating. But other symptoms may occur in places other than the digestive tract and, therefore, not be associated with CD. Here are some additional signs to look for:

- ▶ Loss of appetite
- ▶ Delayed growth
- ▶ Fatigue
- ▶ Anemia
- ▶ Bone and joint pain
- ▶ Weight loss
- ▶ Irritability
- ▶ Depression
- ▶ Dermatitis herpetiformis (skin rash)

Individuals with type 1 diabetes may also experience unexplained low blood sugar (hypoglycemia) or high blood sugar (hyperglycemia) levels.

response in the small intestine. Eventually, this autoimmune response results in partial or complete flattening of the villi, the tiny, hair-like projections that absorb nutrients from foods. Left untreated, the malabsorption of nutrients sets off a constellation of maladies from skin rashes (dermatitis herpetiformis), chronic fatigue, bone loss, and diarrhea, to reproductive disorders and lymphoma.

Contrary to what was previously believed, occurrence of celiac disease isn't rare, especially among individuals with type 1 diabetes. According to Melissa's gastroenterologist Peter H.R. Green, M.D., professor of clinical medicine at Columbia University Medical Center and director of the Celiac Disease Center in New York City, CD affects as many as 1 in 100 people in the U.S., which corresponds with the rate of incidence in European countries. "Celiac disease is one of the most common inherited disorders a physician is going to see," says Dr. Green. What's more, recent statistics of CD among people with type 1 diabetes are daunting: An estimated 1 in 20 people with type 1 diabetes have CD and as many as 1 in 10 will test positive for transglutaminase IgA autoantibodies (an immune marker indicating a propensity for celiac disease and often an early sign the disease is present)—far higher than in the general population.

WHEN CELIAC SYMPTOMS ARE SILENT

Despite the high incidence of CD, the disease often goes undiagnosed and, consequently, untreated. Experts say that it's easy for parents and even physicians to blame the gastrointestinal problems associated with CD (i.e., stomachaches and diarrhea) on other common childhood ailments such as allergic reactions to food. In children with type 1 diabetes, some of the disease hallmarks, such as weight loss and stunted growth, are attributed to poor glycemic control by parents and physicians.

"Children can be quite sick when they are diagnosed with type 1 and in many instances they still have to go to the hospital for initial care," says Marian Rewers, M.D., Ph.D., director of the Clinical Division of the Barbara Davis Center for Childhood Diabetes in Denver. "But that's not the case with celiac disease. It's more like a chronic disease that has a very slow onset and after several years of problems, parents may take their kids from one doctor to another and use a lot of resources and still the child is often misdiagnosed as having food allergies or eczema."

▶ **Melissa & Renee Bennett**

CLICK HERE FOR INFORMATION ABOUT CELIAC DISEASE AND TYPE 1 DIABETES

Numerous online resources provide information and guidance about celiac disease and gluten-free diets. Here are some of the organizations and their Web sites:

Celiac Disease Center

www.celiacdiseasecenter.com

Affiliated with Columbia University Medical Center in New York City, this site provides general information about celiac disease (CD), links to gluten-free diet plans and online grocery stores, support groups, and more.

Celiac.com

www.celiac.com

This comprehensive Web site has a message board for members, an FAQ section and dozens of links to gluten-free bookstores, online gluten-free cooking classes and recipes, support groups and the latest research.

Celiac Disease Foundation

www.celiac.org

This nonprofit organization is primarily for people diagnosed with CD-related dermatitis herpetiformis. Here you'll find general information about CD, an online support community, and links to clinical research and patient care.

The National Institute of Diabetes and Digestive and Kidney Diseases

<http://digestive.niddk.nih.gov>

Part of the National Institutes of Health, this government site has an A-Z Guide to Digestive Diseases. Just click on the Celiac Disease link for general information about the disease, treatment, and other autoimmune diseases associated with CD.

The Gluten-Free Pantry

www.glutenfree.com

This site is dedicated to helping people eat well-balanced gluten-free meals. Gluten-free and low-carb products are available here. Visitors can also join a taskforce to advocate for legislation to reform food-product labeling practices.

While some patients exhibit severe signs of CD such as constant diarrhea, abdominal pain, and anemia, others may not exhibit the classic symptoms at all. According to Dr. Green, many people in the United States (including individuals with diabetes) have "silent celiac" and are not being diagnosed with the disease. "The reason that they have silent CD is that the disease is probably milder. To have diarrhea you've got to have the bulk of your small intestine involved and we have about 22 feet of small intestine as adults. CD is a proximal disorder so the first couple of feet may be involved and people might have anemia or osteoporosis because of the malabsorption of the single nutrients," he explains. "But they won't have diarrhea because sugars and fats can still get absorbed further down the intestine. If you don't have diarrhea it means that you don't have much celiac disease involving the length of the intestine."

CONNECTING CELIAC DISEASE TO TYPE 1 DIABETES

Why CD is so common in people with type 1 diabetes is a question that's capturing significant research attention. Like type 1 diabetes, celiac disease is a genetic, immune-mediated disease—at least in part the result, researchers say, of a clustering of shared Human Leukocyte Antigen (HLA) and non-HLA susceptibility genes triggering an inflammation response. "I think it's the HLA genes plus a few other genes that are involved in immune response," says Marian Rewers, "Just like for type 1 diabetes, investigators are doing complete human genome scans for genes that are associated with celiac disease and several of those genes seem to overlap with diabetes as well as other autoimmune diseases, such as Addison's and thyroid. It's likely that some of the same genes are involved in all of those diseases. What may make the difference is really what the environmental factors are and how they operate under this genetic background, and at what age they trigger the process."

According to Dr. Green, there are two peak times of CD onset, one in childhood from around three to five years of age and one in adulthood during the 30s and 40s. The disease affects many more women, "by a ratio of two or three to one," than men, although it's not clear why. Other than diet, it's unclear what additional environmental factors might be involved in setting off the disease.

Dr. Rewers heads up two ongoing studies that may provide answers. The Celiac Disease Autoimmunity Research (CEDAR) study is investigating the genetic and environmental causes of CD through the prevalence of antiendomysial antibodies (EMA) in at-risk children based on their family histories for type 1 diabetes and/or celiac disease, or genetic susceptibility. Another study under way at the Barbara Davis Center in Denver is the Diabetes Autoimmunity Study in the Young (DAISY). "DAISY is looking for environmental causes for type 1 diabetes, but in doing that we screened newborns and the child population [in Colorado] for genes that increase the risk for both type 1 diabetes and celiac disease," says Dr. Rewers.

"About three years after DAISY was funded, we responded to a request for applications to study the genetic and environmental causes of celiac disease and that's how CEDAR started. And CEDAR led to a couple of other grants from the National Institutes of Health to look closer at celiac disease as a disease that is often associated with type 1 diabetes."

ROUTINE SCREENING: THE BEST NEXT STEP

Some of the long-term consequences of untreated celiac disease involve a litany of serious ailments, including chronic hypoglycemia in those with type 1 diabetes (resulting in compromised neurological function), osteoporosis, and infertility, as well as an increase in potentially life-threatening diseases like small bowel non-Hodgkin's lymphoma and cancers of the mouth, pharynx, and esophagus. It's because of these grave health ramifications that many gastroenterologists as well as other clinicians and researchers are now urging mandatory CD screening for patients with type 1 diabetes, which includes a blood test to determine whether the marker for transglutaminase IgA autoantibodies is present, followed by an upper endoscopic biopsy.

One of the earliest calls for screening came in a 2001 study published in the *Journal of Pediatric Gastroenterology* by researchers

at the Medical College of Wisconsin in Milwaukee. “There had been many European studies showing the high incidence of celiac disease in children with diabetes, but there have only been a couple of studies done in the U.S. And those studies showed a much lower incidence, so we decided to do a better study,” says Steven Werlin, M.D., professor of pediatrics at the Medical College of Wisconsin. The researchers reported that at least 4.6 percent of children with type 1 diabetes had symptoms of CD, with more showing early indicators and signs of the disease. More recent research indicates the percentage is even higher—with 12 to 15 percent of patients with type 1 diabetes having CD or the IgA autoimmune markers, according to George Eisenbarth, M.D., executive director of the Barbara Davis Center for Childhood Diabetes. [The recent data translate to between 1 in 20 with the disease and 1 in 10 with the IgA antibodies.]

“Of the 50 people polled, 75 percent said that their pediatric endocrinologist never asked their child about digestive problems, bowel habits, or energy levels.”

While some centers for childhood diabetes have already begun routine screening for CD, Renee Bennett urges parents of children with type 1 diabetes to be particularly vigilant in spotting the symptoms of CD and to insist on screening. (See “What to Look For,” on page 37.) “I’m shocked that no one over all the years, none of the endocrinologists, ever asked, ‘Does Melissa seem unusually tired, does she sleep a lot, does she have stomachaches?’ because I would have said ‘yes,’” says Bennett.

Earlier this year, Bennett decided to work toward convincing pediatric endocrinologists about the importance of screening for CD even in the absence of conventional symptoms. She designed a survey and sent it to parents whose children have type 1 diabetes and celiac disease. The results, she says, are startling. Of the 50 people polled, 75 percent said that their pediatric endocrinologist never asked their child about digestive problems, bowel habits, or energy levels. Sixty-five percent of respondents said that when their children did complain of stomachaches, they were attributed to blood glucose fluctuations. Only 4 of those polled mentioned their child had suffered from the most often cited sign of CD, diarrhea. In most cases the child’s CD was discovered through blood test results showing elevated levels of IgA antibodies and confirmed by intestinal biopsies.

“Most of the children in the survey were diagnosed with CD within four years of their diabetes diagnosis,” says Bennett. “Only 2 of the 50 were diagnosed with celiac first, so if the CD hadn’t been detected through routine blood work, where would these children be six or seven years from now?”

THE CONTROVERSY OVER SCREENING

The long-term consequences of asymptomatic, or silent, CD remain unclear. Certainly, adhering to a severely restricted gluten-free diet puts an extra burden on children already coping with type 1 diabetes. But, most experts agree that screening, diagnosing, and treating

CD—regardless of symptoms—will help prevent serious health complications.

“We know that untreated celiac disease may not become symptomatic until you’re an adult and then it can become symptomatic with a whole bunch of different complications,” says Dr. Werlin. “So the pediatric GI world is united. Everybody agrees that children with diabetes should be screened.”

Whether to routinely screen type 1 patients for CD, as well as strategies for better managing the disease and recommendations for future research, will be announced this summer at the National Institutes of Health Consensus Development Conference on Celiac Disease in Bethesda, Maryland, when celiac experts from around the world meet.

Now a junior at Barnard College in New York City, Melissa Bennett has been on a gluten-free diet—the only available treatment for celiac disease—since last fall. While her symptoms have improved, she admits sticking to the diet is challenging. “There’s definitely a learning curve with the diet. I still have more fatigue than I think is normal, so I think my diet isn’t 100 percent gluten-free. I could be getting gluten from things I don’t know contain it.” As a result of her undiagnosed CD, Melissa is now contending with osteopenia (decreased calcification or density of bone).

Perhaps soon, with increased awareness of and testing for the disease, patients with type 1 diabetes won’t have to suffer for years with undiagnosed celiac disease and will instead reap the health benefits from early diagnosis and treatment. ●

LIVING GLUTEN-FREE

The only available treatment for celiac disease is the complete elimination of wheat, rye, barley, and possibly oat grains from one’s diet. But the same general rules for maintaining a healthy diet and good blood glucose control still apply: Eat a variety of foods, including ones rich in fiber such as fresh vegetables and fruit; count carbohydrates; limit your intake of fats and sweets; and eat several small meals a day.

“The general view is that the diet has to be gluten-free and patients have to do carbohydrate counting so they can either regulate their glucose levels with insulin injections or a pump,” says Anne Lee, MS.Ed, R.D., a certified diabetes educator and nutritionist at the Celiac Disease Center at Columbia University Medical Center in New York City. “One of the pitfalls is that a lot of the gluten-free products tend to have lower complex carbohydrates, so they have a higher glycemic index as well as a higher fat content. As a result they don’t fit in the normal carbohydrate exchanges because we have to manipulate those. {to writer: please clarify} What we encourage patients to do is not to eat traditional gluten-free foods, but to go back to good basic whole foods that use some of the other grains like buckwheat and millet, because they’re a better fit.”

And, Lee warns patients to watch out for foods and products with hidden gluten. For example, many brands of soy sauce contain gluten as do some medications and food additives like flavorings and colorings. “You have to read labels very carefully. For a lot of products you have to call the manufacturer to make sure of all the ingredients. It becomes so problematic.”

A registered dietician or nutritionist can help patients sort through the food maze as well as help to determine fat, carbohydrate, and other nutritional needs.