

impact



THE UNIVERSITY OF CHICAGO
CELIAC
DISEASE CENTER

IMPROVING LIVES THROUGH AWARENESS,
EDUCATION, AND RESEARCH

Refractory Celiac Disease: What is it? What to do?

Carol Semrad, MD

Celiac disease is an inflammatory disease of the small bowel triggered by wheat, rye and barley in the diet. Diagnosis is made by a small intestinal biopsy that shows characteristic inflammatory changes and flattening of the lining that reverts back to normal on a gluten-free diet. Positive specific antibodies (tissue transglutaminase, endomysial, or deamidated-gliadin peptide) and the HLA DQ2 or DQ8 genotype are supportive of the diagnosis. Greater than 90% of those with celiac disease have improvement in symptoms within two weeks of starting a gluten-free diet. However, restoration of the small intestinal lining to normal may take up to 2 years due to the variable amount of time needed to completely exclude gluten from the diet.

About 10% of patients diagnosed with celiac disease do not get better on a gluten-free diet. This can be due to many different reasons. The most common is dietary indiscretion (unintentional or intentional), because gluten is present in so many foods and medications. Another common cause is lactose or fructose intolerance due to increased ingestion of milk and fruit to compensate for the inability to eat wheat products. Both sugars are more difficult to absorb when compared to table sugar. Occasionally, the problem can be attributed to

a missed diagnosis, detected upon re-review of the intestinal biopsy. Less common causes include food allergy, small bowel bacterial overgrowth, decreased pancreatic digestive enzymes, collagenous sprue (collagen deposit under the small intestinal lining cells) or microscopic colitis (inflammation beneath the colon lining cells). In the latter, the colon appears normal and requires colonic biopsies for diagnosis. Very rarely, individuals produce antibodies against their small intestinal lining cells so-called autoimmune enteropathy. Positive anti-enterocyte or anti-goblet cell antibodies and biopsy findings of cell death (apoptosis) in the regenerating lining cells (crypt cells) or loss of goblet (mucous-producing cells) are signature features.

When all other causes for failure to improve on a gluten-free diet have been excluded, refractory celiac disease (sometimes called refractory sprue) should be considered. Refractory celiac disease is defined as symptoms and small intestinal inflammation that persist after one year on a strict gluten-free diet. Some patients never respond to a gluten-free diet, others initially responded but have a recurrence of symptoms and intestinal inflammation. Refractory sprue appears to be typical of adults, especially middle-aged or elderly people, and is never encountered in the pediatric population.

The question of whether those who never initially responded to a gluten-free diet truly have celiac disease continues to be debated. In recent studies, almost all those with



Carol Semrad, MD

refractory disease carry the HLA DQ2 or DQ8 genotype and most have a positive antibody study before starting a gluten-free diet to suggest an association with celiac disease. Most individuals with refractory disease have diarrhea, malabsorption and weight loss as well as vitamin and mineral deficiencies. In those with severe symptoms, repeat small intestinal biopsy to evaluate for refractory disease is performed earlier than one year after diagnosis.

Refractory celiac disease is divided into two types based on special studies or flow cytometric analysis of lymphocytes performed on small intestinal biopsies. Patients with Type I have a normal T-cell population interspersed along the intestinal lining and usually have a good response to treatment with steroids or azathioprine and a good prognosis. Those with Type II have an abnormal T-cell population interspersed along the intestinal lining, respond poorly to steroid treatment, often require intravenous nutrition, and have a high chance of developing T-cell lymphoma. In those with a high number of abnormal lymphocytes,

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University of Chicago Comer Children's
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Hepatology and Nutrition

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The University of Chicago Celiac Disease Center is dedicated to raising awareness rates and meeting the needs of people affected by celiac disease nationwide through education, research and advocacy.

The contents of this newsletter are not intended to diagnose or recommend treatment for celiac disease. Please consult your healthcare provider with questions about your condition.

For more information about the University of Chicago Celiac Disease Center, please contact our office:

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chemotherapy and bone marrow transplantation have been tried with some success to prevent progression to lymphoma.

There are now new technologies available to examine the entire small bowel for ulcerations, lymphoma or carcinomas in those with refractory disease or alarm symptoms (abdominal pain, bleeding, weight loss) in celiac disease. Capsule endoscopy is a pill containing a camera that is swallowed. As it makes its way through the digestive track, it videotapes the entire small intestine. Double

Balloon Enteroscopy is a long, specialized endoscope that also allows full examination of the small bowel but has the added advantage of obtaining biopsies and marking abnormal areas.

It is important to keep in mind that celiac disease poorly responsive to a gluten-free diet is rarely due to refractory disease or lymphoma. Other explanations are much more likely. A repeat small intestinal biopsy is often helpful because a significantly improved or normal biopsy virtually excludes the diagnosis of refractory celiac disease.

A DREAM COME TRUE: THE CELIAC DATABASE

It has been a longstanding goal of Celiac Center founder Dr. Stefano Guandalini to create a database of all celiac patients seen at the University of Chicago Medical Center, both adults and children. The purpose of such a database would be to be able to spot common trends among the population that could eventually lead to new avenues of research or treatment possibilities.

Twenty-four donors at our April fundraising event, Spring Flours, have made the celiac database a reality. We raised over \$12,000 earmarked for the project, and it is already underway. The database is being designed inhouse by the University of Chicago information services experts, and we have two highly dedicated volunteer interns who are organizing and inputting the data. The entire project is being spearheaded by Dr. Stacy Kahn, a pediatric gastroenterologist at the University of Chicago.

We hope this project will be completed over the next few months. A special thanks to all of our donors, and to our wonderful interns, Janelle Porter and Carly Silverman. We couldn't do it without you!

Annual Celiac Center Blood Screening Coming Up

The Celiac Center's Annual Celiac Disease Center Blood Screening is just around the corner! It will take place on Saturday, October 18, from 8:30 am until noon. There will also be a Q & A panel answering audience questions about celiac disease from 10:30 am until 11:30 am, and a number of different vendors distributing or selling samples of their gluten-free products.

While the panel is open to the public, preregistration for the screening is mandatory. Anyone with a risk factor for celiac disease is eligible for testing, as long as you are on a



Janelle Porter and Carly Silverman get the celiac database underway!

diet that contains gluten. Risk factors for celiac disease include:

- A close family member with biopsy-confirmed celiac disease
- Type I diabetes, or a close family member with Type I diabetes
- Down syndrome
- Thyroid disease
- Chronic gastrointestinal symptoms
- Abdominal bloating and pain
- Chronic fatigue
- Small stature
- Failure to thrive (children only)
- Anemia that does not respond to iron therapy

To register for the screening, please call our office at: (773) 702-7593. We will go through a series of questions with you to determine your risk factor(s) for celiac disease. Registration closes on October 15 or sooner, if it fills up. We thank Prometheus Laboratories for their generous sponsorship—without their support, this event would not be possible.

CELIAC CENTER'S NETWORK OF SPECIALISTS

With so much expertise at the University of Chicago Medical Center, we have assembled a Network of Specialists—physicians at the University of Chicago in various specialties who are aware of celiac disease and cognizant of their specialty's tie-ins with it. The doctors on the list, which is constantly being reviewed and expanded, are:

Carol Semrad, M.D.

Associate Professor of Medicine
Department of Medicine, Division of
Gastroenterology

Director, Adult Clinical Nutrition

For an appointment, please call:
(773) 702-6140.

David P. Cohen, M.D.

Associate Professor of Obstetrics/
Gynecology Chief,
Reproductive Endocrinology and
Infertility

For an appointment, please call:
(773) 702-6642.

John Hart, M.D.

Professor of Pathology

Rebecca Lipton, Ph.D.

Associate Professor Endocrinology
Community Health Sciences,
The Institute for Molecular
Pediatric Sciences

Vesna Petronic-Rosic, M.D., MSc

Assistant Professor and Clinic Director
Section of Dermatology

For an appointment, please call:
(773) 702-1161.

Louis H. Philipson, MD

Professor, Endocrinology, Diabetes &
Metabolism

Department of Medicine

For an appointment, please call:
(773) 702-6222 for adults and
(773) 834-0934 for pediatrics.

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Peapod Makes GF Shopping Easy

Peapod, the online grocery delivery company that started in Chicago in 1989, is now expanding its gluten-free shopping. Go to Peapod's website, www.peapod.com, and type "gluten free" in the search field. Peapod will list its dedicated gluten-free brands, such as Enjoy Life and Glutino, as well as other gluten-free options. You can order online and specify your delivery time within a two-hour window, and your gluten-free foods come right to your door. Peapod now operates throughout Chicago, Milwaukee and southeastern Wisconsin, as well as up and down the east coast, from Massachusetts to Virginia.

What makes Peapod different from other gluten-free stores, or from the gluten-free products offered at a regular supermarket or health food store? "We can create stores within a store," explains Peapod vice president Tony Stallone. "So we created a gluten-free store. Our goal is to provide a whole family solution to the problem of getting gluten-free products, and to let people know they no longer need to drive long distances. We can bring their gluten-free food right to their door, along with everything else they need."

How does Peapod decide on what products to add to the gluten-free mix? It works closely with its distributor, says Stallone, and listens carefully to customer feedback and suggestions, which can be submitted over the website. "We are continually adding products," says Stallone. "We want to be a destination for people, to help them prepare meals and enjoy their lives more."

For customers in the Greater Chicago/Milwaukee area, Peapod will soon be carrying fresh baked goods, including gluten-free bread, rolls, brownies, chocolate chip cookies and biscotti, provided by Rose's Wheat Free Bakery in Evanston, IL. Availability will begin in mid-August; see the Peapod website for more details. Peapod hopes to find other local, fresh baked goods suppliers in their other markets, particularly the Boston and the Washington areas, soon.

For more information, visit the Peapod website. And start enjoying the easy life—gluten-free foods brought to your doorstep! Type in the code GLUTENFREE for \$15 off of your first order.

Did you know that you can honor a special occasion or a loved one's memory with a donation to the University of Chicago Celiac Disease Center? For a minimum donation of \$25, we will send a card acknowledging the donation to anyone you choose. You can make a donation online (just specify the recipient in the appropriate space) at www.CeliacDisease.net, or by calling our office at (773) 702-7593 or sending us a check. Please be sure to specify whether the donation is in someone's honor or in someone's memory, and we will send a card to the recipient the same day. Or you can purchase a packet of cards (\$250 for 10), and send out the acknowledgement yourself. Please let us know if you would like blank cards, honor cards, memory cards or any combination at all.

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Raymond P. Roos, M.D.

Marjorie and Robert E. Straus
Professor in Neurological Science
Department of Neurology
For an appointment, please call:
(773) 702-6222 for adults and
(773) 834-8064 for pediatrics.

David Rubin, M.D.

Assistant Professor of Medicine
Department of Medicine, Division of
Gastroenterology Program Director,
Fellowship
in Gastroenterology, Hepatology, and
Nutrition
For an appointment, please call:
(773) 702-6140.

Peter Joseph Smith, M.D.

Assistant Professor of Pediatrics
Developmental/Behavioral Pediatrics
For an appointment, please call:
(773) 702-3095.

Linda Wagner-Weiner, MD

Assistant Professor, Rheumatology,
Department of Pediatrics
La Rabida Children's Hospital &
Research Center

Darrel Waggoner, M.D.

Assistant Professor of Human
Genetics and Pediatrics
Medical Director Department
of Human Genetics

Visit
www.CeliacDisease.net
for the latest news and
information

Call our hotline with
questions:
773-702-7593

PRECEPTORSHIP PROGRAM

One of the cornerstones of our mission is our commitment to educating doctors and other medical professionals about celiac disease. The University of Chicago Celiac Disease Center's Third Annual Preceptorship Program, a two-day all expense paid intensive course on celiac disease, will take place on December 4th and 5th. We are currently accepting applications for the Preceptorship Program. Doctors in all specialties, nurse-practitioners and dietitians are eligible. Please visit our website at <http://www.celiacdisease.net/preceptorshipprogram> for more information, and for the Preceptorship application.

This year's Preceptors will meet and observe our founder and noted pediatric gastroenterologist Dr. Stefano Guandalini, as well as other specialists from the Celiac Center's Doctor's Network. They will hear lectures on how the various specialties, such as endocrinology, pathology and neurology, are connected with celiac disease. They will also have a session with dietitians Lara Field and Elizabeth Wall on the gluten-free diet.

We hope to record all Preceptor lectures and sessions, to create the first online Continuing Medical Education course for doctors everywhere. This will expand the educational opportunities exponentially in the area of celiac disease for medical professionals all over the U.S. and the world, and will lead to improved diagnosis and ongoing care for celiac patients everywhere.

Research Studies From Around the World

The University of Chicago Medical Center does some of the most cutting edge celiac disease research in the world. However, no one institution can work on every aspect of celiac disease all the time. To that end, the physicians affiliated with the University of Chicago Celiac Disease Center keep us posted when an interesting or relevant study is performed on celiac disease elsewhere in the world. We post these links, along with the doctors' summaries, on our website at <http://www.celiacdisease.net/studies>. Here is an example of one such submission:

Oral manifestations of celiac disease

A recent article published in the Journal of Clinical Gastroenterology (Pastore et al. 2008, January 24) reviews previously published studies on oral manifestations of celiac disease, and concludes that dental enamel defects are the oral lesions most closely related to celiac disease. There is also an increased incidence of oral aphthae and idiopathic atrophic glossitis but this association is less clear. The authors conclude that patients with systematic dental enamel defects should be screened for celiac disease even in the absence of gastrointestinal symptoms.

Bottom line: *This information is not new, as it was known that such dental defects can be seen often in celiac patients, but it is certainly a welcome refresher to physicians and dentists who seem often times to ignore the close association of enamel defects with celiac disease. And remember: only permanent teeth are affected, so do not look for these changes in your four year old!!*

Leonardo R. Hormaza, M.D.

Title: *Oral Manifestations of Celiac Disease*

Source: http://www.ncbi.nlm.nih.gov/pubmed/18223505?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

Annual Free Blood Screening & Expert Panel Q & A—

Mark Your Calendar Now! The next Annual Blood Screening at the University of Chicago Celiac Disease Center will take place on Saturday, October 18. We will also have a panel discussion when attendees have a chance to ask your questions about celiac disease of the experts, and of course, a chance to enjoy delicious gluten-free products and samples. Pre-registration for the event is required, and will open on August 15. Please see our website, www.CeliacDisease.net, for more details.