



FROM THE NATIONAL DIGESTIVE DISEASES INFORMATION CLEARINGHOUSE

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Intestinal Damage from Celiac Disease Persists in Adults, Even with Gluten-free Diet

For adults with celiac disease, treatment with a gluten-free diet will begin to reduce symptoms such as diarrhea and weight loss within weeks. However, recovery from damage to mucosal tissue that lines the small intestine is much slower. Recent research supported by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) shows that for many adults with celiac disease, tissue damage persists after 5 years of adherence to a gluten-free diet.



Murray and five colleagues from the Mayo Clinic studied the effect of a gluten-free diet on mucosal tissue recovery in a group of 241 adults—176 women and 65 men with an average age of 47—with celiac disease, which had been confirmed by intestinal biopsy. The patients also had follow-up biopsies 2 years and

5 years after diagnosis.

The researchers couldn't identify a common risk factor or other reason why some patients experienced recovery from tissue damage within 2 years, while the condition persisted much

“Good adherence to a gluten-free diet is necessary for mucosal recovery, but doesn't guarantee mucosal recovery in all adults with celiac disease. Mucosal recovery did not occur in a substantial portion of adults with celiac disease for years after diagnosis. The rate of confirmed recovery was only 34 percent at 2 years,” wrote Joseph A. Murray, M.D., of the Mayo Clinic College of Medicine in Rochester, MN. After 5 years on a gluten-free diet, Murray noted, one in three adults with celiac disease still showed intestinal damage. The research findings were reported in the February 9, 2010, advance online issue of *The American Journal of Gastroenterology*.

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Joseph A. Murray, M.D.
Mayo Clinic College of
Medicine, Rochester, MN

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longer in others. Overall, the patients in the study had a 66 percent rate of good adherence to a gluten-free diet—determined through interviews with dietitians—a rate that matches the overall adult rate seen in other studies. For most patients in the study, a gluten-free diet eliminated clinical symptoms such as diarrhea and weight loss. However, only 43 percent of patients who maintained good dietary adherence achieved mucosal recovery. One possible cause of this result, the research group suggested, is inadvertent gluten ingestion from a source that is difficult to identify. “These findings further support the urgent necessity of standard labeling for gluten-free foods in the United States,” the researchers wrote.

A second objective of the study was to evaluate the effect of persistent intestinal damage on patients’ long-term health. The researchers

found that regardless of age or sex, adults with celiac disease whose intestinal tissues experienced recovery were less likely to die from all causes than were men and women with persistent damage. “Achievement of mucosal recovery after treatment with a gluten-free diet in adults with celiac disease may be associated with a better survival compared with patients with persistent mucosal damage. Systematic follow-up with intestinal biopsies may be advisable in patients diagnosed with celiac disease as adults,” the researchers concluded.

More information about research projects funded by the National Institutes of Health can be found by using the Research Portfolio Online Reporting Tools (RePORT) Expenditures and Results (RePORTER) tool located at www.projectreporter.nih.gov/reporter.cfm. The research described in this article is funded under NIDDK grant number 5R01DK057892-08. ■

Would you like to know more about NIDDK-supported research?

The National Institutes of Health (NIH) provides access to a variety of reporting tools, reports, data, and analyses of NIH research activities at the Research Portfolio Online Reporting Tools (RePORT) website, www.projectreporter.nih.gov/reporter.cfm. One of the tools available is RePORT Expenditures and Results (RePORTER), which allows users to search a repository of NIH-funded research projects and access and download publications and patents resulting from NIH funding. ■

CELIAC DISEASE News



Celiac Disease News, an email newsletter, is sent to subscribers by the National Digestive Diseases Information Clearinghouse (NDDIC). The newsletter features news about celiac disease, special events, patient and professional meetings, and new publications available from the NDDIC and other organizations.

Please visit www.celiac.nih.gov/Newsletter.aspx to read or download a PDF version or to subscribe to the newsletter.

The National Institutes of Health Celiac Disease Awareness Campaign provides current, comprehensive, science-based information about the symptoms, diagnosis, and treatment of celiac disease, also known as celiac sprue, nontropical sprue, and gluten-sensitive enteropathy. The Awareness Campaign

is an initiative of the NDDIC, a service of the National Institute of Diabetes and Digestive and Kidney Diseases.

Visit www.celiac.nih.gov to learn more about the Awareness Campaign.

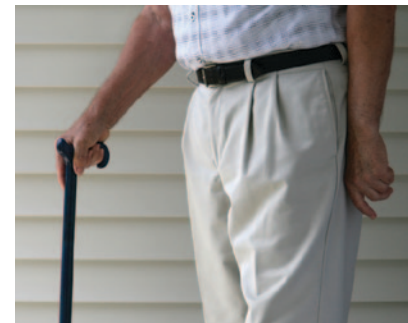
Executive Editor: Stephen P. James, M.D.

Dr. James is the director of the Division of Digestive Diseases and Nutrition within the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). As director, Dr. James oversees planning, implementation, and evaluation of a national research effort focused on gastrointestinal, pancreatic, hepatobiliary, and nutrition diseases and conditions. Before joining the NIDDK in 2001, Dr. James directed the division of gastroenterology at the University of Maryland’s School of Medicine for 10 years.



Celiac Disease Associated with Increased Risk of Neurological Problems in Adults

Celiac disease appears to be associated with increased likelihood of developing neurological problems that include migraine, carpal tunnel syndrome, and movement disorders such as unsteadiness and impaired gait, according to a study by a group of European researchers. Moreover, the researchers found more than a third of the adult celiac disease patients they studied reported experiencing depression, personality change, or psychosis. The study results were published in the November 16, 2009, issue of *Movement Disorders*.



“The prevalence of neurological manifestations and celiac disease is striking and must be considered more than accidental.”

Katrin Burk, M.D.
University of Marburg,
Germany, and colleagues

The study involved 72 adults—10 men and 62 women ranging in age from 36 to 66—with biopsy-confirmed celiac disease and adherence to a gluten-free diet. The participants underwent a neurological examination and completed a questionnaire that provided information about their neurological and general medical history.

More than a fourth—28 percent—of the study participants had a history of migraine. “In many cases, there was a decrease of the frequency and intensity of migraine attacks after the introduction of a gluten-free diet,” wrote lead researcher Katrin Burk, M.D., of the University of Marburg in Germany.

The neurological history questionnaire also revealed that more than a third of study participants had a history of psychiatric disorders. “Interestingly, 35 percent of patients with celiac disease report a history of psychiatric disease, including depression, personality change, or even psychosis,” Burk wrote. Twenty percent of participants reported suffering from carpal tunnel syndrome, and 8 percent had episodes of dizziness associated with inner ear or vestibular problems.

The neurological examination found that more than one-quarter of participants had problems with stance and gait and 35 percent had impaired

proprioception—the sensory “feedback” loop that continuously monitors the relative positions and movements of body parts. Roughly 13 percent of participants showed impairment of the vestibular-ocular reflex, which coordinates information received from the inner ear with muscles that move the eye in order to keep objects of interest in the center of the field of vision when the head is moving.

“Taken together, we found a high frequency of proprioceptive and vestibular deficits leading to problems of stance and gait. The prevalence of neurological manifestations and celiac disease is striking and must be considered more than accidental. It is true that pathogenic mechanisms linking celiac disease to the nervous system have not yet been identified. Obviously, the patients’ gluten-free diet had resolved intestinal symptoms, but had not prevented the development of neurological deficits,” Burk and colleagues concluded.

Because participants in the study had no signs of nutritional deficiencies due to malabsorption, the link between the observed neurological disorders and celiac disease is likely associated—at least in part—with immune-related inflammatory changes throughout the central and peripheral nervous systems, Burk and colleagues speculated. ■

Increased Testing Triples Detection of Celiac Disease in Children

The use of antibody testing to detect celiac disease has led to a dramatic increase in diagnosis in North American children, according to data reported by a research group at the University of Calgary, Canada. The findings were reported in the December 2009 issue of *Pediatrics*.

“The introduction of serological testing led to a marked increase in recognition of the diversity of celiac disease clinical presentations, particularly in older children.”

Kelly McGowan, B.H.Sc.
University of Calgary, Canada,
and colleagues

The group found that the incidence of celiac disease diagnosis more than tripled—going from 2.0 per 100,000 to 7.3 per 100,000—in children younger than age 18 following the 1997 introduction of testing for immunoglobulin A endomysial antibody (IgA-EMA). Moreover, the average age at diagnosis more than quadrupled, going from 2 years to 9 years. Both the increase in incidence and the increase in average age at diagnosis reflect improved ability to detect celiac disease in children with a wide range of symptoms, the researchers said.

“The marked increase in the incidence of celiac disease between time periods can be attributed to the improved detection of nonclassic presentations, particularly in older children. Improved physician awareness through educational programs and increased emphasis on celiac disease in the medical literature likely contributed to that,” wrote Kelly McGowan, B.H.Sc., principal author of the research report.

McGowan and University of Calgary colleagues Derek Castiglione and J. Decker Butzner, M.D., evaluated data compiled by the Alberta Children’s Hospital on children younger than age 18 who were diagnosed with celiac disease through intestinal biopsy. The children were divided into two groups: a pretesting group comprising children diagnosed between 1990 and 1996 and a testing group diagnosed between 2000 and 2006. The researchers’ aim was to assess how the initiation of IgA-EMA testing would affect the incidence of diagnosed childhood celiac disease and the symptoms of children diagnosed with the disease.



Symptoms were classified as classic—diarrhea with failure to thrive or weight loss exceeding 10 percent; atypical—including any gastrointestinal symptoms such as diarrhea, vomiting, abdominal pain, or constipation without weight loss or failure to thrive; extraintestinal—defined on the basis of symptoms, such as anemia, that did not involve the gastrointestinal tract; and silent—asymptomatic but with risk factors such as family history or type 1 diabetes.

Among the pretesting group of 36 children diagnosed with biopsy-confirmed celiac disease, 67 percent presented with classic symptoms, 19 percent had atypical symptoms, 14 percent had extraintestinal symptoms, and none were classified as silent. The overall percentage of classic symptoms among children diagnosed between 2000 and 2006—after the initiation of IgA-EMA testing—was only 19 percent, although these symptoms predominated in children younger than age 3. Among older children in the testing group, atypical and silent presentations were predominant. Silent presentation accounted for 28 percent of all diagnoses in the testing group.

“The introduction of serological testing led to a marked increase in recognition of the diversity of celiac disease clinical presentations, particularly in older children. Many children with atypical gastrointestinal presentations and those in high-risk groups with mild symptoms were recognized because of serological testing,” the researchers concluded. ■

NIH and FDA Announce Partnership to Speed New Treatments to Patients

The U.S. Food and Drug Administration (FDA) and the National Institutes of Health (NIH) have launched an initiative designed to accelerate the process from scientific breakthrough to the availability of new, innovative medical therapies for patients. The collaboration combines the NIH's vast experience supporting and facilitating new discoveries in the laboratory and clinic with the FDA's more than 100 years of experience and knowledge in the regulation and approval of drugs, biologics, and medical devices.



“Collaboration between NIH and FDA, including support for regulatory science, will go a long way to foster access to the safest and most effective therapies for the American people.”

Kathleen Sebelius
Secretary, U.S. Department of Health and Human Services

The initiative involves two interrelated scientific disciplines: translational science, the shaping of basic scientific discoveries into treatments, and regulatory science, the development and use of new tools, standards, and approaches to more efficiently develop products and more effectively evaluate product safety, efficacy, and quality. Both disciplines are needed to turn biomedical discoveries into safe and beneficial treatments.

The agencies will establish a Joint NIH–FDA Leadership Council to spearhead collaborative work on important public health issues. The Joint Leadership Council's work will help ensure that regulatory considerations form an integral component of biomedical research planning and that the latest science is integrated into the regulatory review process.

In addition, the NIH and the FDA will jointly issue a Request for Applications, making

\$6.75 million available over 3 years for work in regulatory science. The research supported through this initiative should add to the scientific knowledge base by providing new methods, models, or technologies that will inform the scientific and regulatory community about better approaches to evaluating safety and efficacy in medical product development.

“We've all been following the remarkable advances in biomedical sciences led by the NIH with great enthusiasm for years,” said U.S. Department of Health and Human Services Secretary Kathleen Sebelius, who announced the initiative on February 24, 2010. “However, much more can be done to speed the progress from new scientific discoveries to treatments for patients. Collaboration between NIH and FDA, including support for regulatory science, will go a long way to foster access to the safest and most effective therapies for the American people.” ■

NIDDK Celebrates 60 Years of Research to Improve Health



“We celebrate the Institute’s accomplishments over the past 60 years in supporting and conducting research on some of the most common, chronic, and costly diseases affecting people in this country and around the world.”

Griffin P. Rodgers, M.D., M.A.C.P.
Director, NIDDK

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) was established 60 years ago by President

Harry S. Truman. In announcing activities that will mark the Institute’s anniversary, NIDDK Director Griffin P. Rodgers, M.D., M.A.C.P., said, “We celebrate the Institute’s accomplishments over the past 60 years in supporting and conducting research on some of the most common, chronic, and costly diseases affecting people in this country and around the world, as well as on diseases and disorders that are less widespread but nonetheless devastating in their impacts.”

As part of the commemoration of the NIDDK’s 60th anniversary, the Institute published *NIDDK: 60 Years of Advancing Research to Improve Health*, which highlights the Institute’s research accomplishments and describes its current efforts and future plans. The publication is available to read or download at www2.nidDK.nih.gov/AboutNIDDK/ReportsAndStrategicPlanning/SixtiethAnniversary. A video highlighting select advances from the 60th anniversary publication is available at www3.nidDK.nih.gov/video/60_anniv.



The NIDDK also has announced a schedule of special events to commemorate the anniversary. Among these activities is the NIDDK’s scientific symposium “Unlocking the Secrets of Science: Building the Foundation for Future Advances,” which will be held in Bethesda, MD, on September 21, 2010. More information about this and other activities is available at www2.nidDK.nih.gov/60thAnniversaryEvents.htm. ■

NIDDK Information Products Receive 14 Plain Language Awards

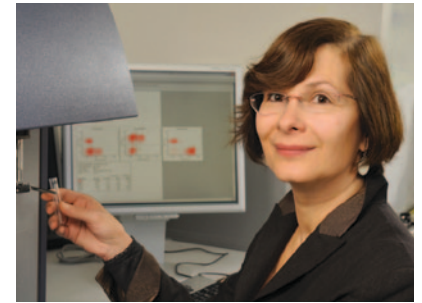
National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) publications, websites, and other informational products have been honored with 14 National Institutes of Health (NIH) Plain Language Awards. The annual awards program, now in its 10th year, honors communication products that help the NIH reach all Americans with health information they can use and research results they can easily understand.

NIDDK resources—including publications, radio reports, and web-based materials—received five Bronze, five Silver, and four Gold awards. The winning publications included easy-to-read materials designed for Spanish- and Vietnamese-speaking audiences.

More than 300 nominations were submitted for this year’s awards, and the winners were announced during a ceremony May 26. Information about the NIH Plain Language Awards program and a list of winning entries is available at www.nih.gov/clearcommunication/plainlanguage.htm. ■

NIDDK-supported Celiac Disease Researcher Wins International Award

Bana Jabri, M.D., Ph.D., has been awarded the coveted William K. Warren Jr. Prize for Excellence in Celiac Disease Research. Jabri is co-director of the University of Chicago Digestive Disease Research Core Center, whose research is supported in part by National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) grants.



Presented annually by The William K. Warren Foundation, the \$25,000 prize is awarded internationally to an individual or group who has made a significant contribution to the field of celiac disease research through basic, translational, or clinical research. Jabri is the first U.S. researcher to receive the Warren Prize.

Jabri's research led to the development of techniques for using mice in celiac disease research. Her team of researchers introduced

genetic modifications in mice that removed their tolerance to gluten—a breakthrough that is now being used to create a mouse model of the human disease. Research on the genetically altered mice will lead to a better understanding of the pathogenesis of celiac disease and will speed development and evaluation of new therapies.

Visit <http://celiaccenter.ucsd.edu/research.shtml> to learn more about the Warren Prize. ■

NIDDK Scientist Elected to American Academy of Arts and Sciences

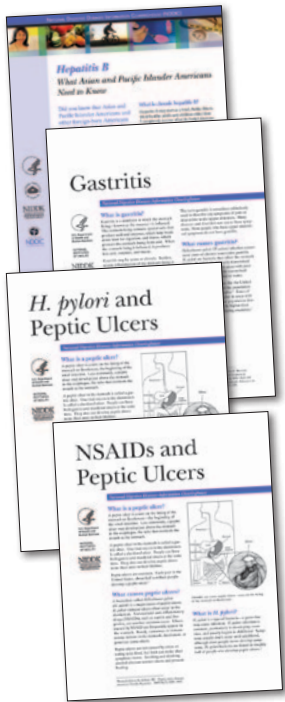
G. Marius Clore, M.D., Ph.D., chief of the National Institute of Diabetes and Digestive and Kidney Diseases' (NIDDK's) Protein Nuclear Magnetic Resonance Section, was elected a member of the American Academy of Arts and Sciences. Each year the Academy, founded in 1780, elects a class of men and women of exceptional achievement in science, scholarship, business, public affairs, and the arts to conduct projects and studies responsive to society's needs and problems. Visit www.amacad.org to learn more about the Academy. ■



NIDDK Publication Highlights Research Advances



NIDDK Recent Advances and Emerging Opportunities, published each year since 2001, provides examples of the research advances made by National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)-funded scientists and their colleagues in the most recent fiscal year. The 2010 publication includes "Stories of Discovery," which trace progress in specific research areas, and "Patient Profiles," which tell patients' personal stories. The publication is available to read or download at www2.niddk.nih.gov/AboutNIDDK/ResearchAndPlanning/Advances/FY2010/default.htm. ■



Additional Resources

New and Updated Publications

Hepatitis B: What Asian and Pacific Islander Americans Need to Know

This new fact sheet explains why Asian, Pacific Islander, and other foreign-born Americans are at higher risk for chronic hepatitis B and describes how to protect against hepatitis B. Available in English, Chinese, Korean, Vietnamese, and Tagalog. Go to www.digestive.niddk.nih.gov/ddiseases/pubs/HepB_AP/index.htm.

Gastritis

This updated fact sheet provides information about the various causes of gastritis and tests used to diagnose it. Go to www.digestive.niddk.nih.gov/ddiseases/pubs/gastritis.

H. pylori and Peptic Ulcers

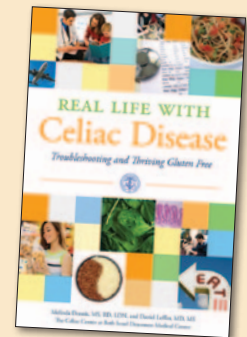
This updated fact sheet provides information about peptic ulcers and how *H. pylori* bacteria can cause them, diagnosis, and treatment. Go to www.digestive.niddk.nih.gov/ddiseases/pubs/hpylori.

NSAIDs and Peptic Ulcers

This updated fact sheet provides information about the relationship between nonsteroidal anti-inflammatory drugs (NSAIDs), such as aspirin and ibuprofen, and peptic ulcers; symptoms; diagnosis; treatment; and long-term outlook. Go to www.digestive.niddk.nih.gov/ddiseases/pubs/nsaids. ■

New American Gastroenterological Association Book Provides Glimpse of *Real Life with Celiac Disease*

A new book from the American Gastroenterological Association (AGA) offers a broad selection of practical knowledge about celiac disease and gluten-related disorders. The book was created to help people living with celiac disease—and those who remain undiagnosed—achieve the best possible health and well-being, the AGA says. The authors—Melinda Dennis, M.S., R.D., L.D.N., and Daniel A. Leffler, M.D., M.S.—are co-founders of the Celiac Center at Beth Israel Deaconess Medical Center in Boston. Visit www.gastro.org/patient-center/digestive-conditions/celiac-disease to learn more about *Real Life with Celiac Disease*. ■



Upcoming Meetings, Workshops, and Conferences

The National Institute of Diabetes and Digestive and Kidney Diseases Information Clearinghouses will exhibit at the following upcoming events:

American Academy of Family Physicians Scientific Assembly

September 29–October 2 in Denver.

For more information, visit www.aafp.org/assembly/2010.

American Academy of Pediatrics National Conference and Exhibition

October 2–5 in San Francisco.

For more information, visit www.aapexperience.org.

American College of Gastroenterology Annual Scientific Meeting and Postgraduate Course

October 15–20 in San Antonio.

For more information, visit www.acg.gi.org/acgmeetings.

American Dietetic Association Food and Nutrition Conference and Expo

November 6–9 in Boston.

For more information, visit www.eatright.org/fnce. ■