News and Resources from the National Institutes of Health

Digestive Diseases
NEWS
National Digestive Diseases Information Clearinghouse
Winter 2007

NIDDK Explores Causes, Treatment, and Research Challenges for Acute Liver Failure

Researchers from several continents convened in Bethesda, MD, in December to share knowledge about the causes, management, and prevention of acute liver failure (ALF) and to make recommendations for future basic and clinical research.

ALF affects an estimated 2,000 people in the United States annually and is due to a variety of causes that result in the same clinical condition characterized predominantly by severe liver test abnormalities and often accompanied by multiorgan failure. The causes of ALF vary from country to country even though the clinical manifestations remain the same, according to William M. Lee, M.D., a professor at the University of Texas Southwestern Medical School in Dallas.

For example, acetaminophen overdosing accounts for about half of all adult ALF cases in the United States but is a virtually unknown cause in India. Because of these disparate causes, "multicenter studies and possible international studies are the best way to go about addressing this disease," Lee said at a 2-day meeting sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

Research Progress

ALF research was limited by the disease's rarity until about 1998, when the Acute Liver Failure Study Group (ALFSG), funded by the NIDDK and headquartered at the University of Texas Southwestern Medical Center, began collecting detailed prospective information and biosamples on more than 1,100 patients from more than 20 U.S. medical centers. ALF is now studied by separate adult and pediatric study groups comprising 23 medical centers for recruiting adults and 18 for recruiting children.

The University of Texas Southwestern Medical Center continues to serve as the Data Coordinating Center for the adult ALF study group and the University of Pittsburgh for the pediatric study group. Both the adult and pediatric study groups have three major goals:

- to collect detailed data
- to perform ancillary studies
- to perform therapy trials

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National Institute of Diabetes and Digestive and Kidney Diseases

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The ALFSG is nearing completion of a clinical trial begun in 1999 to test the effectiveness of n-acetyl cystiene (NAC) for treating ALF cases not due to acetaminophen overdose. Final results from the trial are expected at the end of 2007.

"Liver transplant represents a lifesaving therapy for patients with severe, medically unresponsive ALF."

Timothy Davern, M.D.
Assistant professor, University of California at San Francisco, Department of Medicine

NAC treatment is highly effective for acetaminophen overdose, but doctors must administer the treatment "urgently" because it is most effective when taken as soon after the overdose as possible, according to Timothy Davern, M.D., assistant professor in the Department of Medicine at the University of California at San Francisco (UCSF).

Davern pointed out that while medical treatment for ALF is currently limited, "liver transplant represents a lifesaving therapy for patients with severe, medically unresponsive ALF." The 1-year survival rate for these patients following a liver transplant is better than 90 percent at UCSF, according to Davern.

Liver transplantation is responsible for improving the outcome of ALF from nearly 100 percent mortality to the current overall mortality rate of 40 percent, according to Lorenzo Rossaro, M.D., professor of medicine in the Department of Internal Medicine and Transplant at the University of California at Davis Medical Center.

Complicating Factors

Pursuing a liver transplant for a person with ALF is a complex process because

- prognostic scores for demise due to ALF are imperfect
- the availability of a liver donor organ is unpredictable
- a liver transplant in people who would have survived without a transplant subjects them to the morbidity associated with lifelong immunosuppression
- spontaneous survival is possible even with advanced ALF

Future Research

Research on ALF treatment, according to meeting attendees, is or should be headed toward

- determining which perturbations in homeostatic mechanisms drive the clinical syndrome of ALF
- discovering and developing novel, mechanistically designed agents aimed at limiting hepatocyte injury and death and promoting hepatic repair and regeneration
- prospective studies of long-term outcomes that explore the persistence or recurrence of liver disease, general health status, neurological sequelae, and quality of life of people who recover from ALF
- long-term outcomes of the live donors of liver transplants for ALF
- identifying specific interventions to avoid liver transplantation in defined subgroups
- developing accurate markers to predict liver recovery to avoid unnecessary transplantation
- developing clinically effective liver support and assist devices

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Digestive Diseases
NEWS

NDDIC
Information Clearinghouse
www.digestive.niddk.nih.gov

Digestive Diseases News, an email newsletter, is sent to subscribers four times a year by the National Digestive Diseases Information Clearinghouse (NDDIC). The newsletter features news about digestive diseases, special events, patient and professional meetings, and new publications available from the NDDIC and other organizations.

If you would like to subscribe, send an email to *niddk@info.niddk.nih.gov*. You can read or download a PDF version of the newsletter at *http://digestive.niddk.nih.gov/about/newsletter.htm*.

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

Stephen P. James, M.D., 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 Awareness Campaign Gains Visibility

"Of Guts and Gluten: In Celiac Disease, the Two Don't Mix" was the front-page feature in the November 2006 issue of the *NIH News in Health* newsletter.

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Celiac Disease Awareness Campaign is gaining visibility in the national media and within the National Institutes of Health (NIH) since its official launch on July 18.

In addition to being mentioned in a November 1, 2006, article on celiac disease in *USA Today*, the NIH and its Awareness Campaign received press from WABC New York Radio, PR Newswire—which reaches small and large media markets nationwide—and the *NIH News in Health*.

The NIDDK also created three public service announcements about the Awareness Campaign for its XM Satellite Radio Spanish Project and staffed exhibit booths featuring Awareness Campaign materials at the

- American Dietetic Association Annual Meeting in Honolulu, September 16 to 19
- American Academy of Family Physicians Scientific Assembly in Washington, DC, September 27 to October 1
- American College of Gastroenterology Annual Scientific Meeting in Las Vegas, October 20 to 25
- International Celiac Disease Symposium in New York City, November 9 to 11

Media attention and public outreach efforts continue to increase the visibility of the National Institutes of Health (NIH) Celiac Disease Awareness Campaign. Recent coverage included

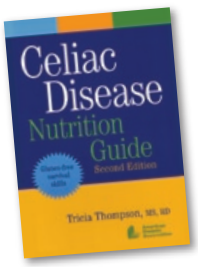
- a *USA Today* article on celiac disease that referenced the Awareness Campaign
- press from WABC New York Radio
- PR Newswire
- *NIH News in Health*, a monthly newsletter

Speaking Out

At the International Celiac Disease Symposium, Stephen James, M.D., director of the NIDDK Division of Digestive Diseases and Nutrition, gave two presentations about the formation, activities, and progress of the Awareness Campaign to scientists, health care professionals, and people with celiac disease. Frank Hamilton, M.D., NIDDK digestive diseases program branch chief, spoke about celiac disease and the Awareness Campaign on NIH Research Radio in August and at the 29th Annual Celiac Sprue Association Conference in Green Bay, WI, in October.

The NIDDK continues to promote the Awareness Campaign website, *www.celiac.nih.gov*, and newsletter. The most recent issue of *Celiac Disease News*, as well as a newsletter archive and newsletter subscription form, is posted at *www.celiac.nih.gov/news.aspx*. ■

Featured in the NIDDK Reference Collection



Celiac Disease Nutrition Guide

Can I eat oats? How do I know I'm getting the nutrients I need? Anyone seeking comprehensive dietary information about celiac disease will find the *Celiac Disease Nutrition Guide* a useful resource. Produced by the American Dietetic Association, the second edition of this guide includes food guidelines for a gluten-free diet, sample menu ideas for main meals and snacks, tips for eating away from home, names and addresses of mail-order companies that sell gluten-free products, and a variety of resources for additional information. Visit *www.catalog.niddk.nih.gov/resources/detail.cfm?pubid=11198* for information on how to order the guide. ■

Study Examines Racial Differences in Response to Hepatitis C Therapy

African Americans with chronic hepatitis C genotype 1 had half the response rate of non-Hispanic Caucasians to combination drug therapy, which could not be explained by clinical patient characteristics, disease severity, or amount of medication taken, according to a recent study published in *Gastroenterology*.

Researchers often attribute the poor response to hepatitis C therapy to a failure to take the full doses of interferon and ribavirin. The side effects of these drugs can be troublesome, causing patients to reduce or discontinue the medication. In this study of 196 African Americans and 205 Caucasians, 36 percent of the patients had at least one dose reduction, while 17 percent discontinued therapy early.

About 3.2 million Americans have chronic hepatitis C virus (HCV) infection, which is the leading cause of chronic liver disease and the most common cause of liver transplantation in the United States.

However, drug reduction and discontinuation rates were similar among African American and Caucasian participants, making the changes in prescribed medication doses an unlikely reason for the racial differences in medication response rate, according to the study.

Even after controlling for important factors associated with a combination therapy response, race was an independent determinant of response.

Ongoing Studies

Ancillary studies to address these potential causes for nonresponse are ongoing, according to Charles Howell, M.D., chairman of the Virahep-C Steering Committee, who discussed the results at the Digestive Diseases and Nutrition subcommittee meeting during the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Advisory Council Meeting in September.

The study, "Peginterferon and Ribavirin Treatment in African American and Caucasian American Patients With Hepatitis C Genotype 1," was a multicenter treatment trial that

recruited patients at eight U.S. clinical centers between July 2002 and December 2003.

About 3.2 million Americans have chronic hepatitis C virus (HCV) infection, which is the leading cause of chronic liver disease and the most common cause of liver transplantation in the United States.

African Americans have a higher prevalence of HCV infection and are more likely to have genotype 1 than other racial groups, according to the study. Yet despite this prevalence, African Americans have been underrepresented in most hepatitis C therapy trials, making it hard to estimate response rates accurately within this population.

More information on chronic hepatitis C is available from the National Digestive Diseases Information Clearinghouse *at www.digestive.niddk.nih.gov/ddiseases/pubs/chronichepc.* ■

NIH Awards $117 Million to Bolster Biomedical Research

Multidisciplinary Centers to Study Liver Disease, Obesity, Diabetes

The National Institutes of Health (NIH) will fund two new Centers of Biomedical Research Excellence (COBRE) to study liver disease, and obesity and diabetes as part of the Institutional Development Award (IDeA) program, an initiative designed to improve investigator competitiveness in states that have been historically underfunded for competitive NIH research.

"The investigators in IDeA states are successfully leveraging NIH's investment by attracting additional funding and expanding their research endeavors."

Elias A. Zerhouni, M.D.
Director of the National Institutes of Health

A new COBRE at Louisiana State University's Pennington Biomedical Research Center will concentrate on obesity and diabetes, and the University of Kansas Medical Center will investigate liver disease. The NIH National Center for Research Resources (NCRR), which awards the funds, also will support new centers at the University of Mississippi to conduct neuroscience research and at the University of Vermont and State Agricultural College to examine infectious pathogens.

Leveraging Investments

"The investigators in IDeA states are successfully leveraging NIH's investment by attracting additional funding and expanding their research endeavors," said NIH Director Elias A. Zerhouni, M.D. "By building on NIH's support, they are also accelerating the pace of research discoveries by making significant contributions to a range of complex health issues, such as increasing our understanding of liver function, the immune system's response to infectious pathogens, and the prevention of heart failure."

Each COBRE includes a principal investigator with established credentials relevant to the center's research theme; three to five individual research projects that share that theme and are supervised by a single junior investigator; and a development and mentoring plan that will prepare these investigators to secure competitive federal research funding.

Projects that will receive continued funding after competitive review include: immunological research at Dartmouth Medical School; cardiovascular investigations at the Medical University of South Carolina; the study of microbial pathogens at the University of Kansas Medical Center; investigations of the central nervous system at the University of New Mexico; neuroscience research projects at the University of Wyoming and the University of Vermont College of Medicine; and cancer studies at West Virginia University.

Visit the NCRR website at *www.ncrr.nih.gov/resinfra/ri_idap.asp* for more information about the IDeA program and COBRE awards. ■

NIH Funds Hispanic/Latino Health Study

Hispanic Community Health Study to Begin in Four Cities

Seven components of the National Institutes of Health (NIH), including the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), are conducting the largest-ever, long-term epidemiological study of health and disease in Latin American populations living in the United States.

"The knowledge gained from this study will benefit not only Hispanic populations but will also enhance understanding of health and disease in other ethnic groups."

Elias A. Zerhouni, M.D.
Director of the National Institutes of Health

As many as 16,000 participants of Hispanic/Latino origin—4,000 at each of four sites—will undergo a series of physical examinations and interviews to help identify the prevalence of and risk factors for a wide variety of diseases, disorders, and conditions, including diabetes and kidney, liver, and heart disease.

The Hispanic Community Health Study, which will focus on Mexican Americans, Puerto Ricans, Cuban Americans, and Central/South Americans, also will assess such risk factors as diet, physical activity, body weight, blood pressure, blood lipids, medication and supplement use, the environment, and health care access.

"The Hispanic population is the largest minority population in the United States, and it is expected to triple in growth by 2050," said NIH Director Elias A. Zerhouni, M.D. "As this population continues to increase—and to experience varying rates of disease—it is vitally important to understand the risk factors and health behaviors that contribute to these diseases. The knowledge gained from this study will benefit not only Hispanic populations but will also enhance understanding of health and disease in other ethnic groups."

For NIDDK fact sheets in Spanish about cirrhosis of the liver, hepatitis, and nonalcoholic steatohepatitis, please visit *www.digestive.niddk.nih.gov/spanish/index.asp*. ■

The NIH will award $61 million over 6.5 years to four field-study sites:

- Albert Einstein College of Medicine of Yeshiva University in Bronx, NY
- Northwestern University in Chicago
- San Diego State University
- University of Miami

The study's data coordinating center will be at the University of North Carolina at Chapel Hill.

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The NIDDK also funds the Drug-induced Liver Injury Network, a five-center network that collaborates on research related to the magnitude, diversity, and mechanisms of drug-induced liver injury.

For more information about NIDDK research on liver diseases, visit *www.niddk.nih.gov/research/resources/resource.asp?program=liver#2*. ■

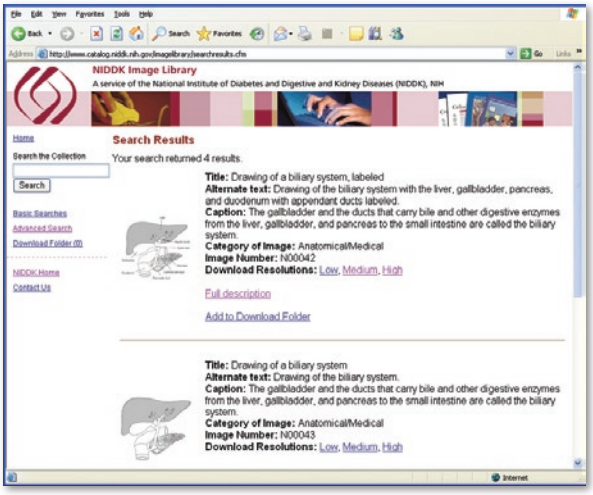
NIDDK Website Offers New Resources

Interactive Health Education Tools and Image Library Now Live

Would you like to watch a video of gallbladder surgery on your computer? Or maybe you're interested in taking an interactive, online tutorial about irritable bowel syndrome.

By visiting *www.digestive.niddk.nih.gov/resources/HealthTools*, a new, interactive section of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) website, you can do those things and much more.

- Test your health knowledge with online quizzes.
- Download digital recordings of radio broadcasts from the National Institutes of Health (NIH).
- Listen to audio files from NIH Research Radio.
- Monitor your health using online diet and exercise tools.



Another new section of the NIDDK website is the Image Library, an online, searchable database of original full-color and black-and-white illustrations produced by the National Digestive Diseases Information Clearinghouse and other NIDDK information clearinghouses.

These tools and resources from the NIH and the National Library of Medicine about digestive diseases are compiled into one section of the NIDDK website for ease in finding and accessing all that is available. Interactive tools are also available for diabetes at *www.diabetes.niddk.nih.gov/resources/HealthTools* and kidney and urologic diseases at *www.kidney.niddk.nih.gov/resources/HealthTools*.

Image Library Live

Another new section of the NIDDK website is the Image Library, an online, searchable database of original full-color and black-and-white illustrations produced by the National Digestive Diseases Information Clearinghouse and other NIDDK clearinghouses. The library organizes the drawings into instructional, anatomical/medical, and lifestyle/activity categories. These illustrations are available copyright-free to the public at no cost, although the NIDDK should be credited as the source of each downloaded illustration. The illustrations are available in high, medium, and low resolutions at *www.catalog.niddk.nih.gov/ImageLibrary*. ■

New NIDDK Website Makes Debut

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) unveiled a new and improved website in September, offering the National Institutes of Health staff, researchers, and the general public more online information and resources in an easier-to-use format.

"Our website is truly the public face of the NIDDK."

Griffin P. Rodgers, M.D.
Acting Director, NIDDK

The website redesign features an improved look, better navigation, and more user-friendly functions. Users who visit *www.niddk.nih.gov* will now enjoy

- new "Scientific Areas" sections that enable researchers to easily find funding areas and opportunities in their field of interest with up-to-the-minute information about
  - special NIDDK initiatives
  - upcoming conferences
  - research resources
  - NIDDK staff contacts
- easier navigation for finding information about the kinds of science the NIDDK funds and instructions necessary for completing the grant application process
- a redesigned health education section for the public with basic information on diseases, along with statistics, links to additional resources, Spanish translations, and lists of available NIDDK publications

Many website improvements also occurred behind the scenes. "The new website now has a database-driven content management system, giving us much better tools to maintain it as a truly living document," said Maren Laughlin, Ph.D., senior adviser for integrative metabolism at the NIDDK. "The new, improved site structure should allow website visitors to more easily see all that is available to them." Laughlin served on the NIDDK 18-member content committee, one of two committees set up to rework the website's extramural sections.

More To Come

The recent facelift is only phase one of a three-part plan to revamp the entire NIDDK website. While the first phase focused on site architecture and updated content, phases two and three will put design and color to work to give the home page and other parts of the site a fresh look.

Final improvements include the addition of multimedia content and more database tools, such as an automated event calendar and an organizational chart to make finding staff contact information easier. Professional and NIDDK web staff also will have new, interactive, electronic tools to help update and maintain the website.

A user survey—the American Consumer Satisfaction Index—reported an 82 percent overall satisfaction rate with the health information sections of the NIDDK website for November 2005 through January 2006.

That score is among the highest achieved by all participants in the survey, which is administered jointly by ForeSee Results and the University of Michigan. The NIDDK redesigned the health information sections 3 years ago and set the standard for this effort.

"Our website is truly the public face of the NIDDK," said NIDDK Acting Director Griffin P. Rodgers, M.D. "It facilitates the conversation that takes place among biomedical researchers at our universities and small businesses, the American public, and the Institute. With this new website, we hope to invite greater participation and better serve our mission of improved health for the American people." ■

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