

Digestive Diseases

NEWS

National Digestive Diseases Information Clearinghouse

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Researchers Explore Improving Long-term Outlook for Children With Liver Transplants

Children who undergo liver transplantation have an excellent outlook for long-term survival, thanks to advances in surgery and drugs to prevent organ rejection. But many challenges may threaten their quality of life along the way, including damage to other organs, post-transplant malignancies, and growth and development difficulties. Improving long-term health outcomes for these children was the subject of a daylong meeting organized by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) in February.

An ongoing concern for researchers and physicians is the effect of immunosuppressive drugs on children. A major challenge of liver transplantation is how to minimize immunosuppression without sacrificing graft function.

The most serious complications of long-term immunosuppression, according to Sue V. McDiarmid, M.D., director of pediatric liver transplantation at the David Geffen School of Medicine, University of California at Los Angeles Medical Center, are

- renal dysfunction due to the use of calcineurin inhibitors
- delays in growth, development, and cognitive function
- new-onset malignancy
- development of increased cardiovascular risk factors
- infection



McDiarmid said the most significant way to improve outcomes after pediatric liver transplantation is to improve immunosuppression. “It would be great to figure out how to withdraw all immunosuppression,” said McDiarmid, who recommended that innovative multicenter trials

focus on the least amount of immunosuppression necessary to achieve good graft function with minimal side effects.

Nonadherence

Nonadherence to immunosuppressive drug regimens because of drug side effects is a research concern that also warrants study. The pediatric liver transplant community is in a unique position to spearhead the study of nonadherence to medical recommendations, the most important risk factor for poor, long-term, pediatric post-transplant outcomes, according to Eyal Shemesh, M.D., assistant professor in the Department of Psychiatry, Pediatrics Division, at Mount Sinai Medical Center.

The most important attribute of the pediatric liver transplantation population is that transplant

LIVER TRANSPLANTATION, continued on page 2

Inside This Issue

Rodgers Named NIDDK Director	3
NIDDK Welcomes Seven New Members to Advisory Council	4
Resources	5
Upcoming Meetings, Workshops, and Conferences	6





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LIVER TRANSPLANTATION, from page 1

centers routinely monitor medication blood levels, according to Shemesh. “Looking at fluctuations in these levels over time provides a powerful, objective, ready-to-use measure of adherence that is unique to this setting.” Other unique attributes, said Shemesh, are that

- pediatric liver transplant centers have agreed on several outcome measures that are routinely collected by most centers, making a multicenter study relatively easy
- specific pilot data about the measurement of adherence, consequences of nonadherence, and even treatment of nonadherence, are available in this population

Positive Outcome Measures

Researchers also should develop more positive diagnostic criteria to measure how well children who receive transplants are doing, rather than using death as the primary measurement, recommended Jay Hoofnagle, M.D., director of the NIDDK’s Liver Diseases Research Branch. Examples of other measures, said Hoofnagle, would be whether the children are going to school, participating in activities, and are later employable.

One of the research goals laid out in the National Institutes of Health (NIH) *Action Plan for Liver Disease Research* is “to define factors associated with successful liver transplantation in terms of growth and development, school performance, and social and intellectual development through a careful prospective and long-term assessment.”

The following websites have more information about liver disease and transplantation:

Immune Tolerance Network
www.immunetolerance.org

Studies of Pediatric Liver Transplantation
<https://web.emmes.com/study/lvr>

Action Plan for Liver Disease Research
<http://catalog.niddk.nih.gov/detail.cfm?ID=766&CH=NDDIC>

NIDDK Liver Transplantation Database
<http://catalog.niddk.nih.gov/detail.cfm?ID=154&CH=NDDIC>

The NIH-funded Studies of Pediatric Liver Transplantation (SPLIT) is a research network comprising 44 pediatric liver transplant centers in the United States and Canada. The network seeks to register and prospectively follow 80 percent of all children receiving a liver transplant to advance clinical research and trials about long-term outcomes, complications, and tolerance.

In addition, the Immune Tolerance Network (ITN) maintains a database and funds many studies on immune tolerance and tolerance-inducing regimens of therapy for kidney, liver, and islet transplantation; autoimmune diseases; and allergies and asthma. The ITN is a joint research network that conducts clinical trials and tolerance assay studies in the areas of kidney, liver, and islet transplantation, autoimmune diseases, and allergies and asthma.

The NIH Action Plan also calls for identifying ways to avoid liver transplantation. For instance, children with biliary atresia—the most common cause of liver transplantation in children—may be able to avoid or delay a transplant through early diagnosis, a successful operation known as the Kasai procedure, and effective anti-cholestatic and anti-fibrotic therapies. ■

Digestive Diseases NEWS



Digestive Diseases News, an email newsletter, is sent to subscribers 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.



Rodgers Named NIDDK Director

National Institutes of Health (NIH) Director Elias A. Zerhouni, M.D., announced the appointment of Griffin P. Rodgers, M.D., as director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) effective April 1, 2007.



Rodgers, who was appointed deputy director of the NIDDK in January 2001, has been the Institute's acting director. Rodgers also has served as chief of the NIDDK's Clinical and Molecular Hematology Branch since 1998.

As NIDDK director, Rodgers oversees an annual budget of \$1.8 billion and a staff of 650 scientists, physician-scientists, and administrators. The Institute conducts and supports research on many of the most serious health issues affecting the public, including diabetes, endocrinology, and metabolic diseases; digestive diseases and nutrition, including obesity; and kidney, urologic, and hematologic diseases.

"Griff Rodgers is an outstanding physician-scientist and molecular hematologist," said Zerhouni. "He has made singular contributions to the study of globin disorders and is internationally recognized for his contributions to the development of effective therapy for sickle cell disease and other genetic diseases of hemoglobin. In addition to his research experience, Dr. Rodgers is a dedicated and knowledgeable clinician and a first-rate research administrator. He has all the qualities we seek in an Institute director."

Rodgers received his undergraduate, graduate, and medical degrees from Brown University. He completed his residency and chief residency in internal medicine at Barnes Hospital and the Washington University School of Medicine. His fellowship training in hematology/oncology was in a joint NIH program with George Washington University and the Washington DC Veterans Affairs Medical Center.

In addition to his medical and research training, Rodgers earned a master's degree in business administration, with a focus on the business of medicine, from the Johns Hopkins University in 2005.

As a research investigator, Rodgers is widely recognized for his contributions to the development of the first effective—and now U.S. Food and Drug Administration-approved—therapy for sickle cell disease. He was a principal investigator in clinical trials to develop therapy for patients with sickle cell disease and also performed basic research that focused on understanding the molecular basis of how certain drugs induce gamma-globin gene expression. He was honored for his research with numerous awards, including the 1998 Richard and Hinda Rosenthal Foundation Award, the 2000 Arthur S. Fleming Award, the Legacy of Leadership Award in 2002, and a Mastership from the American College of Physicians in 2005.

"It is truly an honor to be given the opportunity to lead an organization with a mission as far-reaching and varied as the NIDDK's," said Rodgers. "While the NIDDK has a long and distinguished history of accomplishment as an Institute, we must look to the future to capitalize on the opportunities for disease prevention that new technologies and discoveries are giving us. The health problems we face as a nation are real and the results of research offer substantive promise for solving the difficult questions faced by millions of Americans every day and the health professionals who treat them." ■

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Elias A. Zerhouni, M.D.
NIH Director

NIDDK Welcomes Seven New Members to Advisory Council

Seven new members have joined the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Advisory Council, which met in Bethesda, MD, on February 21. The Council meets three times a year to advise the NIDDK about its research portfolio.

Advisory Council members, who come from the scientific and lay communities, serve 4-year terms and provide second-level peer review of grant applications scored by scientific review groups. Council members are an important liaison between the research communities they represent and the NIDDK, which supports each community's research efforts. The new members are

Charles O. Elson, III, M.D., vice chair for research in the department of medicine and the Basil I. Hirschowitz chair in gastroenterology at the University of Alabama at Birmingham. Elson joins the Digestive Diseases and Nutrition (DDN) Subcommittee.

James W. Freston, M.D., Ph.D., the Boehringer Ingelheim chair of clinical pharmacology and professor emeritus at the University of Connecticut School of Medicine in Farmington. Freston, a member of the NIDDK-funded National Drug-Induced Liver Injury Network, joins the DDN Subcommittee.

Mark A. Magnuson, M.D., the Earl W. Sutherland Jr. professor of molecular physiology and biophysics and director of the center for stem cell biology at the Vanderbilt University School of Medicine in Nashville, TN. Magnuson joins the Diabetes, Endocrinology, and Metabolic Diseases Subcommittee.

William E. Mitch, M.D., the Gordon A. Cain professor of medicine and director of the division of nephrology at Baylor College of Medicine in Houston. Mitch joins the Kidney, Urologic, and Hematologic Diseases (KUH) Subcommittee.



NIDDK Director Griffin P. Rodgers, M.D. (standing front row, second from left), meets with new council members (front row from left) Lisa H. Richardson; William E. Mitch, M.D.; and (back row from left) Anthony J. Schaeffer, M.D.; Mark A. Magnuson, M.D.; James W. Freston, M.D., Ph.D.; Charles O. Elson, III, M.D.; and Patrick Tso, Ph.D.

Lisa H. Richardson, national emeritus chairperson of the board and volunteer for the Crohn's and Colitis Foundation of America. Richardson joins the DDN Subcommittee.

Anthony J. Schaeffer, M.D., the Herman L. Kretschmer professor and chairman of the department of urology at the Feinberg School of Medicine at Northwestern University in Chicago. Schaeffer joins the KUH Subcommittee.

Patrick Tso, Ph.D., professor of pathology, associate director of the Cincinnati Obesity Research Center, director of the Cincinnati Mouse Diabetes Phenotyping Center, and director of the Center for Lipid and Atherosclerosis Research at the University of Cincinnati College of Medicine. Tso joins the DDN Subcommittee.

The Advisory Council will meet again on May 30. ■

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Celiac Disease

What I need to know about Celiac Disease is a 14-page booklet from the National Digestive Diseases Information Clearinghouse (NDDIC) explaining what celiac disease is, its symptoms, how it is diagnosed and treated, and what foods people with celiac disease should avoid. It also describes the Celiac Disease Awareness Campaign, which the NDDIC launched in July 2006 to raise awareness about the disease among health care providers and the public.

Celiac disease is the inability to digest gluten, a protein found in wheat, rye, and barley. An estimated 1 percent of all Americans suffer from celiac disease, though many have never been diagnosed and are not receiving treatment.

Irritable Bowel Syndrome

The NDDIC has also updated the booklet *What I need to know about Irritable Bowel Syndrome*.

Foodborne Illness

The warm-weather season is a time for picnics, cookouts, and other outdoor dining pleasures, but it also is a time to pay special attention to the proper handling, preparation, and storage of food.

Food can become contaminated with bacteria, parasites, or viruses in many ways. For instance, perishable food that is not refrigerated within 2 hours becomes a breeding ground for bacteria, which, if eaten, can cause illness. Although most foodborne illness is not diagnosed or reported, the Centers for Disease Control and Prevention estimates about 76 million people in the United States become ill from pathogens in food each year. Of these, about 325,000 end up in the hospital and 5,000 die. Those at greatest risk are children, older adults, and people with compromised immune systems.

The February issue of the *NIH News in Health* newsletter includes an article that explains the different kinds of germs that can contaminate

Featured in the NIDDK Reference Collection

Children's Liver Association for Support Services

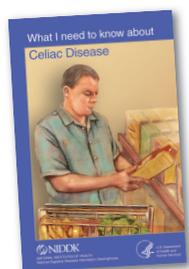
The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Reference Collection has indexed a brochure that familiarizes parents with the Children's Liver Association for Support Services (CLASS), a nonprofit organization dedicated to addressing the emotional, educational, and financial needs of families coping with childhood liver disease and transplantation.

The brochure describes the physiology and role of the liver and lists pediatric liver diseases and common symptoms of liver disease. Symptoms can include jaundice; weakness or excessive fatigue; ascites, or fluid retention in the abdomen; pale stools; firm, enlarged liver; darkened urine; pruritis, or intense itching of the skin; failure to thrive or grow normally; and abnormal bleeding.

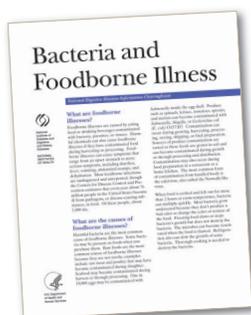
The brochure also describes the activities of CLASS, including the operation of a toll-free information hotline, parent matching for mutual support, a newsletter, a children's website, financial assistance for families of pediatric liver patients, educational materials, and seed grant funding for research projects.

The brochure is available free from CLASS, 26444 Emerald Dove Drive, Valencia, CA 91355, 1-877-679-8256 or 661-255-0353, info@classkids.org.

food and how to prevent foodborne illness. In addition, the NDDIC's updated fact sheet *Bacteria and Foodborne Illness* is available at www.digestive.niddk.nih.gov/ddiseases/pubs/bacteria. ■



To order, please call 1-800-891-5389 or visit <http://catalog.niddk.nih.gov>.



Upcoming Meetings, Workshops, and Conferences

National Commission on Digestive Diseases

The third meeting of the National Commission on Digestive Diseases (NCDD) is scheduled for June 18 to 19 at the Sheraton Crystal City in Arlington, VA. Commission working groups that were assigned specific topics at a previous meeting will present their chapter reports, which will be incorporated into a final Commission report. Congress tasked the NCDD with developing a long-range research plan for digestive diseases. For more details about the meeting, visit the Commission website at www.niddk.nih.gov/federal/ncdd/mtg-info.htm.

NDDIC Information Available at National Exhibits

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) distributes materials and information from its clearinghouses at various conferences throughout the year. Look for the NIDDK, the National Digestive Diseases Information Clearinghouse, or the Celiac Disease Awareness Campaign exhibit booth at the following upcoming conferences:

- American Academy of Nurse Practitioners National Conference from June 20 to 24 in Indianapolis. For more information, visit www.aanp.org/Conferences/2007+Conference/2007+Conference.asp.
- American Academy of Family Physicians Scientific Assembly from October 3 to 7 in Chicago. For more information, visit www.aafp.org/online/en/home/cme/aafpcourses/conferences/assembly.html.
- American College of Gastroenterology Annual Scientific Meeting from October 12 to 17 in Philadelphia. For more information, visit www.acg.gi.org/physicians/education.asp#Annual.

NIDDK Meeting on Fecal and Urinary Incontinence

The National Institutes of Health will hold a “State of the Science” conference on fecal and urinary incontinence December 10 to 12 in Bethesda, MD.

The objective of a “State of the Science” conference is to review information and scientific issues to reach a consensus that will be useful to health care providers and the public. A panel of 14 to 16 broad-based experts hears testimony from issue experts, evaluates the information, and develops responses to a series of predetermined questions. A report from a Technical Assessment Group provides an evidenced-based review of the literature to supplement the process.

Bothersome urinary incontinence affects 14 percent of women of all ages and fecal incontinence affects 2 to 15 percent of all adults. Some of the causes of fecal and urinary incontinence may result from various gastrointestinal disorders and complications of these disorders. These two conditions frequently coexist, especially in older adults and nursing home residents. The estimated economic impact of incontinence is more than \$26 billion annually. Additional information about the conference will be available soon. ■