

Kidney Disease

Research Updates

National Kidney and Urologic Diseases Information Clearinghouse

Fall 2007

NIDDK Director Shares Vision for Kidney Disease Research

Griffin P. Rodgers, M.D., director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH), shares his vision and the Institute's goals for kidney disease research.



As the newly-appointed Director of the NIDDK, I want to underscore the Institute's commitment to vigorous, multipronged research efforts to combat the diseases within our research mission. I am pleased to have the opportunity to share with the nephrology community my vision for the Institute over the next few years.

Chronic kidney disease (CKD), along with end-stage renal disease (ESRD), imposes a tremendous public health burden on Americans. According to the most recent *Annual Data Report* from the United States Renal Data System, patients with CKD or ESRD account for 5.7 and 1.1 percent of the Medicare population, respectively. Together, the treatment of patients with CKD and patients with ESRD accounts for 23.7 percent of Medicare expenditures, making kidney disease an extremely important issue for both research priority setting and public policy considerations.

Diabetes and obesity—diseases within the NIDDK's core mission—may increase the likelihood of developing kidney disease and speed its progression. The NIDDK is particularly concerned about CKD in children, an issue of particular significance given the increasing rates of obesity in this vulnerable population.

The primary scientific programs within the NIDDK's Division of Kidney, Urologic, and Hematologic Diseases (KUH) support basic,

translational, and clinical research; research training and career development; and the dissemination of health information to improve the lives of patients, their families, and those at risk for kidney disease. We will continue to support research that will further evidence-based medicine and promote the translation of research discoveries into medical practice for the direct benefit of patients.

The NIDDK is committed to pursuing the most compelling research to combat kidney disease. In moving this important research forward, several overarching principles will guide my leadership of the Institute:

Maintain a Vigorous Investigator-initiated Research Portfolio. Because the innovation and problem-solving of individual investigators are crucial for research progress, the NIDDK will

KIDNEY DISEASE RESEARCH,
continued on page 2



National Institute of
Diabetes and Digestive
and Kidney Diseases



Inside This Issue

NIDDK RIVUR Study Under Way _____	4
NIDDK Requests for Applications _____	5
NIDDK Convenes Urine Albumin Experts _____	6
NIDDK Unveils Website Makeover _____	7
Featured in the NIDDK Reference Collection _____	8
Additional Resources _____	8



“The ideas and fresh perspectives of new investigators invigorate the research community. Our efforts will include fostering mentorship of new investigators and promoting special consideration for funding talented new investigators.”

Griffin P. Rodgers, M.D.
NIDDK Director

KIDNEY DISEASE RESEARCH, from page 1

maintain funding of investigator-initiated grants at the highest possible level.

One goal is to maximize our investments by supporting cross-cutting science that is broadly applicable to many disease-specific research issues, such as studies of gene-environment interactions and identification of biomarkers to aid in the diagnosis of disease and assessment of new treatments in clinical trials. We will also invest in the novel application of existing technology and development of new technology.

The NIDDK will continue to invest in the development of cell-based therapeutic approaches for repairing damaged tissues and the use of cutting-edge research methods to identify new candidate drugs.

Support Pivotal Clinical Studies and Trials.

Clinical studies will continue to be an integral component of NIDDK kidney disease research. The NIDDK supports studies of patients with acute kidney injury, moderate and severe kidney disease, and those who have progressed to ESRD and dialysis or transplantation. The Institute also funds clinical studies aimed at preventing further complications from initial kidney damage and at improving treatment options for ESRD.

Because kidney disease disproportionately affects minority populations, we will continue to seek insights and answers to health disparities. For instance, one clinical trial is investigating the underlying causes of ESRD to find ways that could slow progression of hypertensive kidney disease in African Americans.

We are also expanding the investigative community's access to very valuable research resources accrued in our major clinical trials. To this end, we are supporting ancillary studies to these trials and a central repository for biologic materials from clinical trials.

Preserve a Stable Pool of Talented New Investigators.

The ideas and fresh perspectives of new investigators invigorate the research community. Our efforts will include fostering mentorship of new investigators and promoting special consideration for funding talented new investigators.

The NIDDK also has a vigorous research career development award program for scientists in the early stages of their careers. These opportunities will be complemented by the NIDDK's participation in NIH-wide efforts that support new investigators, such as the NIH Pathway to Independence Program and the NIH Loan Repayment Program.

Foster Exceptional Research Training and Mentoring Opportunities.

Maintaining an NIDDK-focused pipeline of outstanding investigators is critically important to our research progress against disease. To this end, we offer programs for individuals at different stages in their careers—ranging from those who have already attained advanced degrees to those who are very early in their educational development.

KIDNEY DISEASE RESEARCH,
continued on page 3

Kidney Disease Research Updates



Kidney Disease Research Updates, an email newsletter, is sent to subscribers by the National Kidney and Urologic Diseases Information Clearinghouse (NKUDIC). The newsletter features news about kidney disease, special events, patient and professional meetings, and new publications available from the NKUDIC 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 www.kidney.niddk.nih.gov/about/newsletter.htm.

Executive Editor: Andrew Narva, M.D.

Andrew Narva, M.D., is the director of the National Kidney Disease Education Program (NKDEP) within the National Institute of Diabetes and Digestive and Kidney Diseases. Dr. Narva, a graduate of Harvard Medical School and board-certified in internal medicine and nephrology, served with the Indian Health Service before joining the NKDEP. He also was a member of the National Kidney and Urologic Diseases Advisory Board, the Renal Community Council of the U.S. Renal Data System, the Medical Review Board of End-Stage Renal Disease Network 15, and the National Kidney Foundation's Minority Outreach Committee, which he chaired.



KIDNEY DISEASE RESEARCH, from page 2

We encourage minority investigators to apply for all of our research training and career development awards and also support a Network of Minority Research Investigators to further their long-term academic research careers.

Ensure Knowledge Dissemination Through Outreach and Communications. The NIDDK is committed to translating new knowledge derived from NIH-funded research into better care for people with kidney disease. The NIDDK's National Kidney Disease Education Program (NKDEP) works to reduce morbidity and mortality caused by kidney disease and its complications through educational efforts targeted at communities at risk, patients, and health care professionals.

A critical piece of the Institute's efforts to reduce kidney disease is the ability to assess the burden of the disease in the United States. Therefore, the Institute, along with the Centers for Medicare and Medicaid Services, will continue to support the United States Renal Data System (USRDS). The USRDS is a national data system that collects, analyzes, and distributes information about ESRD in America.

As we plan for the future, we will continue to seek and value external advice from investigators, professional scientific organizations, patient advocates, and the public. Key sources of input will continue to be our National Advisory Council, strategic planning processes, Interagency Coordinating Committees, ad hoc planning groups, and scientific conferences and workshops. This input will provide a useful scientific guidepost as we make resource allocation decisions. Active collaboration with other components of the NIH and other federal agencies will also remain a cornerstone of NIDDK planning efforts. We will continue to seek and value such planning processes as we move forward.

"As we plan for the future, we will continue to seek and value external advice from investigators, professional scientific organizations, patient advocates, and the public."

Griffin P. Rodgers, M.D.
NIDDK Director



The NIDDK is committed to pursuing the most compelling research to combat kidney disease. In moving this important research forward, several overarching principles will guide my leadership of the Institute:

- Maintain a vigorous investigator-initiated research portfolio
- Support pivotal clinical studies and trials
- Preserve a stable pool of talented new investigators
- Foster exceptional research training and mentoring opportunities
- Ensure knowledge dissemination through outreach and communications

Ever-increasing knowledge and the advent of new technologies bring new scientific opportunities for alleviating and conquering the many chronic diseases within the NIDDK's mission. Our continuing goal will be to seize and maximize these opportunities to reduce the burden of disease and improve the public health. To this end, I look forward to working with the NIDDK's many stakeholders in the nephrology community now and in the future. ■

NIDDK RIVUR Study Under Way

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is funding a study that is recruiting 600 children between 2 months and 6 years of age to learn whether all children with vesicoureteral reflux (VUR) should be treated with long-term antibiotics.



For more information about the RIVUR study, visit www.csc.unc.edu/rivur.

The Randomized Intervention for Children with Vesicoureteral Reflux (RIVUR) Study is a randomized, double-blind, placebo-controlled trial of antimicrobial prophylaxis in children with VUR and urinary tract infection (UTI).

VUR is a condition in which urine flows backward from the bladder toward the kidneys during urination. Retrograde urine flow is the most common congenital urologic abnormality in children, according to Marva Moxey-Mims, M.D., director of the NIDDK's Pediatric Nephrology and Renal Centers Programs in the Division of Kidney, Urologic, and Hematologic Diseases.

VUR is found in 30 to 50 percent of children who have had a UTI and is thought to increase the risk of kidney damage when children have recurrent UTIs. At least 1.7 percent of boys and 8.4 percent of girls will have at least one UTI during childhood. Of these, at least 30 percent will have a recurrence.

Renal scarring occurs between 5 and 40 percent of the time and potentially may increase with each UTI. This concerns researchers because scarring can result in reflux nephropathy—kidney damage caused by retrograde urine flow—progressive renal failure, and the eventual need for renal replacement therapy.

The rationale for a multicenter trial is

- lower prevalence of scarring in children
- no drop in the number of VUR patients progressing to ESRD since the 1960s, despite the routine use of prophylactic antibiotics
- invasive, expensive, and stressful diagnostic procedures
- bacterial resistance that can result from long-term antibiotic prophylaxis

Trial participants will have primary VUR documented after the patient's first febrile or symptomatic UTI that is appropriately treated. The trial includes five clinical treatment centers:

- Children's Hospital of Philadelphia, Ron Keren, M.D., principal investigator
- Children's Hospital of Pittsburgh, Alejandro Hoberman, M.D., principal investigator
- The Johns Hopkins School of Medicine, Ranjiv Mathews, M.D., principal investigator
- Wayne State University School of Medicine, Tej Mattoo, M.D., principal investigator
- Women's and Children's Hospital of Buffalo, Saul Greenfield, M.D., principal investigator

The data coordinating center is at the University of North Carolina, Chapel Hill, Myra Carpenter, Ph.D., principal investigator. For more information about the RIVUR study, visit www.csc.unc.edu/rivur. ■

NIDDK Requests for Applications

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is seeking responses to the following Requests for Applications (RFAs):



The NIDDK posts funding opportunities and notices on its website at www.grants.nih.gov/grants/guide.

Ancillary Studies in the Natural History of Acute Kidney Injury

Description: The primary objective of this grant is to establish an Acute Kidney Injury Natural History Consortium comprised of three to five participating clinical centers (PCCs) and one data coordinating center. Each PCC will be expected to follow 200 to 600 patients with acute kidney injury and a similar number of control subjects for up to 4 years for the development or worsening of chronic kidney disease and selected cardiovascular complications. The NIDDK will commit \$2 million annually for 5 years to support the consortium.

Letter of intent deadline: November 26, 2007

Application deadline: December 20, 2007

For more information: <http://grants.nih.gov/grants/guide/rfa-files/RFA-DK-07-009.html>

Identification of Factors Associated with Failure of Arteriovenous Fistulas to Mature in Hemodialysis Patients

Description: This initiative will support a consortium of investigators to conduct a prospective multi-center observational cohort study investigating clinical factors that may be predictive and/or are associated with the failure of newly placed arteriovenous fistulas to mature in patients with end-stage renal disease. The NIDDK will award \$3 million per year for 5 years to create this new research program.

Letter of intent deadline: November 20, 2007

Application deadline: December 13, 2007

For more information: <http://grants.nih.gov/grants/guide/rfa-files/RFA-DK-07-007.html>

Data Coordinating Center for the HALT-Polycystic Kidney Disease Trials

Description: This initiative will support a data coordinating center for the ongoing HALT-Polycystic Kidney Disease (PKD) Trials, which are currently in the enrollment phase. The HALT-PKD trials are investigating the effectiveness of renin-angiotensin-aldosterone system blockade in altering progression of kidney disease in patients with autosomal dominant PKD. The NIDDK will award \$1 million per year to support the data coordinating center. The total project period is 5 years.

Letter of intent deadline: November 20, 2007

Application deadline: December 13, 2007

For more information: <http://grants.nih.gov/grants/guide/rfa-files/RFA-DK-07-008.html> ■

NIDDK Convenes Urine Albumin Experts

Those who oversee programs with implications for the detection and treatment of diabetes, hypertension, and cardiovascular disease are aware that urinary albumin is a key measure for detecting chronic kidney disease (CKD). Most diagnoses of CKD are based on identification of urine albumin, and not on a reduced glomerular filtration rate.

Many health professionals are not aware, however, that various issues prohibit health professionals from obtaining reproducible urine albumin results—a problem with public health, clinical care, and research implications.

For example, if one patient's urine sample was split into three and sent to as many labs, it is possible that a clinician would receive three different results. One reason for this variation: each laboratory can use a different testing method.

Variation in test results is caused, in part, by the lack of availability of a standard method for measuring urine albumin and the lack of materials that can be used to ensure every laboratory gets the same result for a urine sample with a known amount of albumin. Also lacking are agreed-upon ranges and cutpoints for healthy levels of urine albumin for patients of various ages, races, and genders.

These topics are just two of the many measurement and reporting-related issues discussed during a recent meeting of urine albumin experts convened in Washington, DC, by the National Kidney Disease Education Program (NKDEP) and the International Federation of Clinical Chemistry and Laboratory Medicine. Attendees included almost 20 representatives from the National Institutes of Health, the Centers for Disease Control and Prevention, the National Institutes of Standards and Technology, research hospitals and institutions, the in vitro diagnostic industry, and other sectors of the clinical chemistry community—each with an established track record of resolving difficult problems faced by the clinical chemistry community. The group outlined related problems and posed strategies that will eventually help redefine who is identified for CKD and how patients are treated.

For more information, contact the NKDEP at nkdep@info.niddk.nih.gov. ■

The group outlined all related problems and posed strategies that will eventually help redefine who is screened for CKD and how patients are treated.

Federal Agencies Meet to Discuss Kidney Disease

The Kidney Interagency Coordinating Committee (KICC) held its annual meeting in Bethesda, MD, on June 14. The meeting brought together representatives from more than a dozen federal agencies to share information about their programs and activities related to chronic kidney disease (CKD).

Presentations by representatives from the National Institute of Diabetes and Digestive and Kidney Diseases, Agency for Healthcare Research and Quality, Centers for Disease Control and Prevention, Centers for Medicare and Medicaid Services, Food and Drug Administration, Health Resources and Services Administration, Indian Health Service, and Department of Veterans Affairs sparked discussion about how agencies can work together more effectively.

As a follow-up to the meeting, the National Kidney Disease Education Program (NKDEP) is developing an online resource that will summarize CKD-related activities and contacts within each federal agency to facilitate cross-agency collaboration and communication.

The NKDEP, which coordinated the KICC meeting, has made the meeting minutes available on its website at www.nkdep.nih.gov. ■

NIDDK Unveils Website Makeover

Dynamic graphics and an enhanced layout define the redesigned website launched by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

The NIDDK's website reformat is aimed at best directing the site's users—scientists, health care professionals, and the general public—to the topics and sections they seek.

While the fundamental architecture of information remained stable in the redesign process, the committee advancing the design sought to update the website's look and feel and improve the immediate success of information seekers.

“Our new design should save researchers, health professionals, and the public valuable time finding important scientific and consumer health information,” said NIDDK Director Griffin P. Rodgers, M.D. “We are continually striving to make our resources more readily available to a wider audience and in the latest formats. The website plays a key role in helping to disseminate this information.”

NIDDK Website Features Health Information in Spanish

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) has launched a new portal to feature Spanish-language kidney disease materials and resources on its website.

People looking for information about kidney disease in Spanish can now go directly to the Spanish-language portal page, where they will find an A to Z list of topics and titles. The online system for ordering NIDDK materials now includes descriptions in Spanish of available publications to help visitors choose the resources they want. The National Kidney and Urologic Diseases Information Clearinghouse has 19 publications about kidney and urologic diseases in Spanish and will be adding more in the future, including one-page fact sheets that are part of the NIDDK's Awareness and Prevention Series.

The NIDDK website, which receives nearly 2 million visits per month, scored an 83 out of 100 possible points on the American Customer Satisfaction Index (ACSI) for March to June 2007, making it a top-performing site. The ACSI measures the performance of about 200 private-sector companies and many government agencies. Visitors rate government websites on various components of overall satisfaction, such as ease of search and navigation, look and feel, functionality, and content. Ratings are converted to a score on a 100-point scale using ACSI methodology.

The website features a reference collection, an interactive health tools portal, an image library, and portals containing health information in Spanish. ■



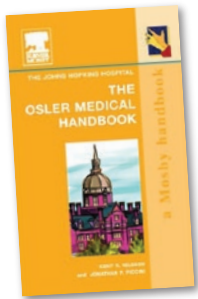
The website features a reference collection, an interactive health tools portal, an image library, and portals containing health information in Spanish.

To visit the site, go to www.niddk.nih.gov.

The new Spanish-language portal is available at www.kidney-espanol.niddk.nih.gov.

The NIDDK website also links to the Spanish-language portal for MedlinePlus and the NIDDK Reference Collection, a free, online database that includes 78 resources in Spanish.

To help people order materials in Spanish, two full-time bilingual information specialists respond to requests for health information. In the past 12 months, more than 17,500 Spanish-language publications were ordered through the three NIDDK Clearinghouses. The NIDDK responded to more than 700 information requests in Spanish during that time. ■



For more information about the handbook, go to www.catalog.niddk.nih.gov/resources and search for “acute renal colic” in “kidney and urologic diseases.”

Featured in the NIDDK Reference Collection

Acute Renal Colic

Acute renal colic is defined as the painful episode that results from a urinary or kidney stone moving through the urinary tract. This chapter on acute renal colic is from the *Osler Medical Handbook*, which provides the essentials of diagnosis and treatment, as well as the latest in evidence-based medicine, for residents working at the bedside. Essential “Fast Facts” and “Pearls and Pitfalls” are useful to the practicing internist. Four sections, Epidemiology, Clinical Presentation, Diagnosis, and Management, cover topics such as the terms used for kidney and urinary tract stones; the use of noncontrast helical computed tomography (CT) as the gold standard for diagnosis of stones; the indications for urgent intervention, including acute kidney failure, high-grade obstruction of a single or transplanted kidney, concurrent urinary tract infection (UTI) with obstruction, and intractable symptoms; management of patients who do not meet the criteria for urgent intervention; and elective removal of urinary tract stones. A list of references is included, each labeled with a “strength of evidence” grade to help readers determine the type of research available in that reference source. For more information about the handbook, go to www.catalog.niddk.nih.gov/resources and search for “acute renal colic” in “kidney and urologic diseases.”

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Reference Collection is a free, online database that helps health care professionals, health educators, patients, and the general public find educational materials not typically referenced in most databases. Visit the collection for additional resources about kidney disease. ■

Additional Resources

New Interactive Tools

New to the Interactive Health Education Tools section of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) website are the following podcasts:

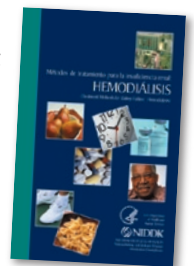
- NKDEP Encourages Awareness About Kidney Disease
- Long-term Study of Health and Diseases in Hispanic Populations (Kidney Disease)
- High Blood Pressure Awareness

The NIDDK interactive tools section consolidates all the tools and resources about kidney disease from the National Institutes of Health and the National Library of Medicine. To access these resources, visit www.kidney.niddk.nih.gov/resources/HealthTools.

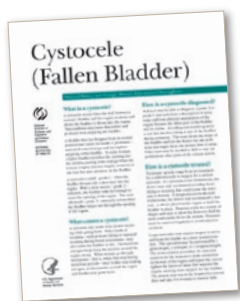
Hemodialysis

A Spanish version of the booklet entitled *Treatment Methods for Kidney Failure: Hemodialysis* is available from the National Kidney and Urologic Diseases Information Clearinghouse.

Hemodialysis is the most common method of treating advanced and permanent kidney failure. Since the 1960s, when hemodialysis first became a practical treatment for kidney failure, hemodialysis treatments have become more effective and side effects have been minimized. This 26-page publication describes how hemodialysis works and addresses related issues such as necessary equipment and procedures, diet, financial issues, and adjusting to changes during treatment. To read or download a copy of the booklet, go to www.kidney.niddk.nih.gov/spanish/pubs/hemodialysis.



ADDITIONAL RESOURCES,
continued on page 9



This fact sheet is available at www.kidney.niddk.nih.gov/kudiseases/pubs/cystocele.

ADDITIONAL RESOURCES, from page 8

Cystocele

This updated fact sheet explains what causes a cystocele, options for treatment, and resources to consult for more information. A cystocele occurs when the wall between a woman's bladder and her vagina weakens and allows the bladder to droop into the vagina. The condition can range from mild, grade 1—when the bladder droops only a short way into the vagina—to grade 3, when the bladder bulges out through the vaginal opening. This fact sheet is available at www.kidney.niddk.nih.gov/kudiseases/pubs/cystocele.

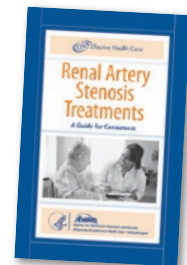
Kidney Disease and African Americans

African Americans are disproportionately affected by kidney failure due, in part, to higher rates of diabetes and high blood pressure—the two leading causes of kidney failure—among this population. Yet many people with these conditions do not know they are at risk. The National Kidney Disease Education Program has a free brochure that explains the connection between diabetes, high blood pressure, and kidney disease. The brochure, *Kidney Disease: What African Americans Need to Know*, encourages African Americans to talk with their doctor or nurse about getting tested for kidney disease. It also lists steps people can take to keep their kidneys healthier longer. For a copy of the brochure, go to www.nkdep.nih.gov.



Renal Artery Stenosis

The Agency for Healthcare Research and Quality (AHRQ) has produced plain-language guides for consumers and health care providers outlining the latest scientific evidence on treatments for renal artery stenosis, the most common cause of correctible high blood pressure.



The consumer guide includes basic information about treatment options and a comparison of treatment risks, including the impact on blood pressure and kidney function. The clinician guide includes more detailed information about these topics and “confidence ratings” of treatment evidence.

The guides are part of the AHRQ's Effective Health Care program series, which will publish similar guides summarizing evidence on oral diabetes medications. For copies of the guides, visit www.effectivehealthcare.ahrq.gov/reports. ■