News and Resources from the National Institutes of Health

Urologic Diseases Research Updates

National Kidney and Urologic Diseases Information Clearinghouse Fall 2007

Sling Surgery More Effective than Burch Technique for Female Bladder Control

The largest and most rigorous U.S. clinical study of two operations for stress urinary incontinence (SUI) in women found the sling procedure helps more women achieve bladder control than the Burch technique, according to the National Institutes of Health (NIH).

The Stress Incontinence Surgical Treatment Efficacy Trial (SISTEr) found that significantly more women with a sling made from a patient's own tissue and placed around the urethra for extra support were dry, compared with women with a Burch colposuspension, in which sutures are attached to a pelvic ligament to support the urethra.

Two years after surgery, 47 percent of women who had the sling procedure and 38 percent who had the Burch technique remained dry from leakage caused by stress or, possibly, urge incontinence. For stress-specific leakage only, 66 percent of women with a sling and 49 percent with a Burch procedure remained dry.

Stress incontinence is when coughing, laughing, sneezing, running, or lifting heavy objects causes urine to leak from the bladder. Urge incontinence is the sudden feeling of the need or urge to urinate. The most common cause of urge incontinence is inappropriate bladder contractions.

SISTEr randomized 655 women with either pure SUI or a combination of stress and urge incontinence to receive a fascial sling or the Burch procedure. Complete information on the measures used to assess urinary incontinence was available for 520 participants—79 percent—2 years after surgery. The study also accounted for quality of life issues, patient satisfaction, and side effects.

While most women in the study were satisfied with the treatment results, those who received a sling were significantly more satisfied—86 percent compared with 78 percent of the Burch group.

However, positive results of the procedure were tempered by side effects, which were more common among women with slings. The most common side effect was urinary tract infection, which occurred in 63 percent of women who had a sling and 47 percent who had the Burch procedure.

Fourteen percent of women with a sling versus 2 percent of women with the Burch procedure also had more voiding problems, and 27 percent versus 20 percent had persistent urge incontinence. Nineteen women with slings who had difficulty voiding after treatment needed surgery to correct the problem; no one in the Burch group needed corrective surgery for voiding problems.

Urinary incontinence is a common and costly condition that reduces quality of life. According to the National Institute of Diabetes and Digestive and Kidney Diseases' (NIDDK)

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National Institute of Diabetes and Digestive and Kidney Diseases

National Institutes of Health

Department of Health & Human Services, USA

Sling Surgery, from page 1

Urologic Diseases in America project, up to 75 percent of U.S. women have some degree of incontinence, costing $12.4 billion in 1995.

SUI is commonly treated with surgery to support the bladder neck and urethra. Randomized, controlled trials comparing these operations are rare. Studies predating SISTEr were small, short-term, or less stringent about diagnostic criteria and outcome measures, producing inconsistent results across studies. SISTEr set a higher bar by standardizing definitions, clinical evaluations, and surgical procedures at all sites and by using "composite outcome measures and a more rigid definition of success compared with other studies," according to the study's authors.

"For the first time, we have a meticulous, relatively long-term comparison of these common surgeries in women."

Leroy M. Nyberg Jr., Ph.D., M.D.
NIDDK Director, Urology Research

This higher bar may account for lower success rates in SISTEr than in earlier trials, but it also "establishes a template for conducting surgical trials for urinary incontinence and for other urological conditions," said John W. Kusek, Ph.D., the NIDDK's co-director of kidney and urology trials.

SISTEr defined two levels of treatment success. Stress-specific success required that women have no leakage symptoms during physical activities, no leakage during a cough stress-test and valsalva—a maneuver performed by forcibly exhaling against closed lips and pinched nose—and no re-treatment for the problem. Overall success required that women meet SUI-specific treatment goals, have a negative pad test, and have no leakage episodes recorded on a 3-day voiding diary.

"For the first time, we have a meticulous, relatively long-term comparison of these common surgeries in women," said Leroy M. Nyberg Jr., Ph.D., M.D., director of urology research at the NIDDK. "Women who participated in this study have made it possible for many women with stress incontinence and their doctors to make more-informed choices based on clear benefits, risks, and personal preferences."

The NIDDK, the National Institute of Child Health and Human Development, and the Office of Research on Women's Health at the NIH funded the Urinary Incontinence Treatment Network (UITN), a group of nine clinical centers and a biostatistical center, to conduct a series of rigorous, long-term trials of common incontinence therapies. SISTEr is the first trial completed by the UITN, with two other studies in the wings.

Results of the second trial, the Behavior Enhances Drug Reduction of Incontinence, a study for urge incontinence, are expected later this year. The third study, the Trial of Mid-Urethral Slings, is recruiting patients to compare two minimally invasive surgeries for the treatment of SUI. For more information about the UITN, visit *www.uitn.net*. For a copy of *What I need to know about Bladder Control*, visit *www.kidney.niddk.nih.gov/kudiseases/pubs/bcw_ez*.

Results of the SISTEr study appeared in the May 24 issue of the *New England Journal of Medicine*. ■

Urologic Diseases
Research Updates

NKUDIC
www.kidney.niddk.nih.gov

Urologic Diseases Research Updates, an email newsletter, is sent to subscribers by the National Kidney and Urologic Diseases Information Clearinghouse (NKUDIC). The newsletter features news about urologic diseases, 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*.

Editor: Leroy M. Nyberg Jr., Ph.D., M.D.

Dr. Nyberg is the director of urology and urology centers programs at the National Institute of Diabetes and Digestive and Kidney Diseases, part of the National Institutes of Health (NIH) in Bethesda, MD. Dr. Nyberg is a graduate of Tufts University in Boston, Columbia University in New York, and the University of Massachusetts Medical School in Worcester and completed residency training in urology at The Johns Hopkins Hospital in Baltimore. He has also held faculty positions in urology at The Johns Hopkins Medical School, in urology and biochemistry at the Medical University of South Carolina, and in urology at the University of Connecticut. Dr. Nyberg received the Distinguished Service Award from the American Urological Association for significant clinical and research contributions to urology. He also received the NIH Directors Award for excellence for the development of urologic research programs at the NIH.

NIDDK Director Shares Vision for Urologic Diseases 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 urologic diseases 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 share with the urologic research community my vision for the Institute over the next few years.

Noncancerous or "benign" urologic diseases place a major burden on public health. According to the most recent edition of *Urologic Diseases in America*, bladder, prostate, and other urinary tract diseases cost Americans nearly $11 billion a year in direct medical expenditures. Diabetes and obesity—diseases within the NIDDK's core mission—may increase the likelihood of developing and the speed of progression of benign urinary-associated conditions. Many of these diseases are symptom-based and can be difficult to diagnose, treat effectively, or cure.

The NIDDK's urologic research portfolio includes basic, clinical, and epidemiological research on the genitourinary tract. We have gained important insights from studies on non-cancerous urologic disorders and diseases, including benign prostatic hyperplasia, prostatitis, and erectile and sexual dysfunction. The Institute also funds research into urinary tract infections, urinary tract stone disease, interstitial cystitis, urinary incontinence, pelvic floor disorders, and congenital anomalies of the genitourinary tract.

We will continue to pursue the most compelling research to address these and other debilitating and costly chronic diseases. Moreover, we will remain firmly committed to 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 these diseases.

The following overarching principles will guide my leadership as the new Director of the NIDDK:

Maintain a Vigorous Investigator-initiated Research Portfolio. The NIDDK will maintain funding of investigator-initiated grants at the highest possible level. We will maximize our investments by supporting cross-cutting science that is broadly applicable to many disease-specific research issues. Examples of this research include identification of biomarkers that can aid in the diagnosis of disease and in the assessment of new treatments in clinical trials.

Support Pivotal Clinical Studies and Trials. Clinical studies will continue to be an integral component of research on the broad spectrum of diseases for which the NIDDK has research responsibility. The NIDDK supports a number of clinical trials related to benign urologic diseases, including a clinical network studying treatment approaches to urinary incontinence in women.

Other clinical networks are performing studies on chronic pelvic pain syndrome/chronic prostatitis and new approaches for treating patients with painful bladder syndrome/interstitial cystitis.

Research Goals, continued on page 4

"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."

Griffin P. Rodgers, M.D.
NIDDK Director

Research Goals, from page 3

Preserve a Stable Pool of Talented New Investigators. We will work to ensure that new investigators realize their potential for contributing to biomedical research and that today's generation of young scientists will view research as a viable career. Our efforts will include fostering mentorship of new investigators and promoting special consideration for funding talented new investigators.

A vigorous research career development award program aids 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.

Foster Exceptional Research Training and Mentoring Opportunities. Maintaining an NIDDK-focused pipeline of outstanding investigators is critically important to our research progress. To this end, we offer programs for individuals who are 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.

Ensure Knowledge Dissemination Through Outreach and Communications. We are continuing efforts to ensure that the science-based knowledge gained from NIDDK-funded research is imparted to health care providers and the public for the direct benefit of patients and their families.

The Institute maintains a number of information clearinghouses related to its research mission. For example, the goal of the National Kidney and Urologic Diseases Information Clearinghouse is to increase knowledge and understanding about these diseases among patients and their families, health care professionals, and the general public.

In moving research forward, the following overarching principles will guide my leadership as the new Director of the NIDDK:

- 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.

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.

Active collaboration with other components of the NIH and other federal agencies will also remain a cornerstone of NIDDK planning efforts.

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. ■

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.

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).

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

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

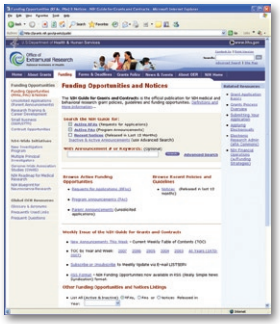
Trial participants will have primary VUR documented after the patient's first febrile or symptomatic UTI that is appropriately treated. The trial includes five clinical treatment centers:

- 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.cscc.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.*

Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network

Description: This initiative will develop a multicenter cooperative research network focusing on urologic chronic pelvic pain syndromes—interstitial cystitis/painful bladder syndrome and chronic prostatitis/chronic pelvic pain syndrome—and their major associated comorbidities. The MAPP Research Network will consist of up to six discovery sites, a data coordinating site, and a tissue analysis and technology site. The NIDDK will provide up to $7.5 million annually for 5 years.

In-person information session: November 5, 2007
Letter of intent deadline: December 17, 2007
Application deadline: January 9, 2008
For more information: *http://grants.nih.gov/grants/guide/rfa-files/RFA-DK-07-003.html*

George M. O'Brien Urology Research Centers

Description: This initiative will support multidisciplinary, basic, translational, and clinical research to improve the diagnosis, detection, and/or treatment of urologic disorders and diseases within NIDDK mission interests. Project goals include having the O'Brien centers integrate urologic research into surrounding institutions, attract new investigators as well as established investigators with new scientific expertise, and provide for regional, national, and international collaborations. The NIDDK will fund up to five awards at a maximum $750,000 per award per year over 5 years.

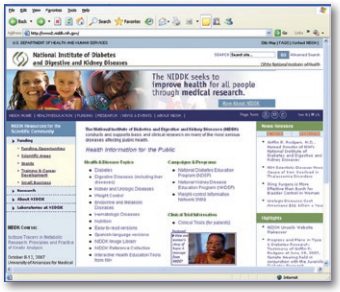
Letter of intent deadline: February 13, 2008
Application deadline: March 13, 2008
For more information: *http://grants.nih.gov/grants/guide/rfa-files/RFA-DK-07-004.html*

Multidisciplinary K12 Urologic Research (KURe) Career Development Program

Description: This initiative will support institutional career development programs in urologic research for M.D.s, Ph.D.s, and M.D./Ph.D.s interested in benign urologic disease or urologic research related to the NIDDK's mission. The individualized career development training offered through these programs will prepare candidates for an independent, clinical, translational, or basic science career in urologic research. The NIDDK will provide approximately $2 million in fiscal year 2008 to support up to three awards. Applicants may request a project period of up to 5 years and a budget of up to $850,000 per year.

Letter of intent deadline: February 19, 2008
Application deadline: March 18, 2008
For more information: *http://grants.nih.gov/grants/guide/rfa-files/RFA-DK-07-006.html* ■

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 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 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.

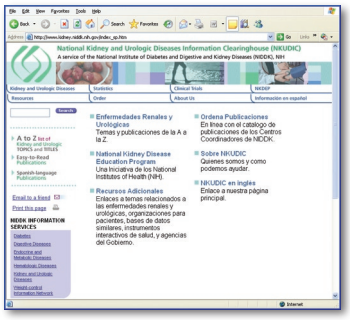
While the fundamental architecture of information remained stable in the redesign process, the committee advancing the design sought to update the website's look and feel and improve the immediate success of information seekers.

"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."

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. ■

NIDDK Website Features Health Information in Spanish



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

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

People looking for information about urologic diseases 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 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. Between July 15, 2006, and June 27, 2007, 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. ■

Patient education materials also can be ordered online by visiting the AUA website at *www.auanet.org/catalog.*

Featured in the NIDDK Reference Collection

Patient Booklets

The American Urological Association (AUA) Foundation has a series of patient education booklets available about urologic health:

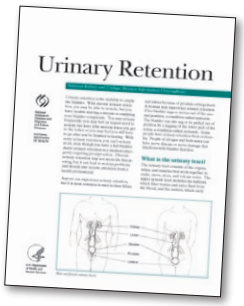
- *A Basic Guide to Bladder Health: How Much Do You Know About Your Bladder?*
- *Benign Prostatic Hyperplasia: Treatment Choices*
- *Enlarged Prostate: Benign Prostatic Hyperplasia*
- *Erectile Dysfunction: Causes, Risks and Talking to Your Doctor*
- *Kidney Stones: Basic Facts Everyone Should Know*
- *Prostate-Specific Antigen*
- *Prostatitis: Symptoms, Causes and Treatments*

Single copies of the booklets are available free by calling or writing the AUA Foundation at 1000 Corporate Boulevard, Suite 410, Linthicum, MD 21090, 1–800–828–7866. For multiple copies, call 410–689–3990.

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. To find more resources about urologic disease, visit *www.catalog.niddk.nih.gov/resources*. ■

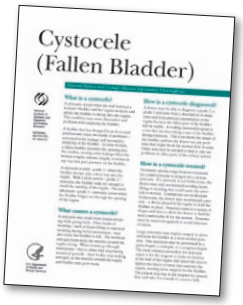
Additional Resources

Urinary Retention



A new fact sheet from the National Kidney and Urologic Diseases Information Clearinghouse explains the symptoms, causes, diagnosis, and treatment of urinary retention, or the inability to empty the bladder. Urinary retention is most common in men in their 50s and 60s due to prostate enlargement. Serious complications can arise from urinary retention, including chronic kidney disease, bladder damage, and urinary tract infections. Copies of the fact sheet are available at *www.kidney.niddk.nih.gov*.

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*.

ADDITIONAL RESOURCES,
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Additional Resources, from page 8

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:

- Streaming audio and podcast about the National Institutes of Health (NIH) report *Urologic Diseases in America*, which found that Americans pay $11 billion a year to treat bladder, prostate, and other urinary tract diseases

The NIDDK interactive tools section consolidates all the tools and resources about urologic diseases from the NIH and the National Library of Medicine, including health quizzes, tutorials, podcasts, streaming audio files, and surgical videos. To access these resources, visit *www.kidney.niddk.nih.gov/resources/HealthTools*.

Upcoming Meetings, Workshops, and Conferences

Fecal and Urinary Incontinence

The National Institute of Diabetes and Digestive and Kidney Diseases and the National Institutes of Health Office of Medical Applications of Research will convene a State-of-the-Science Conference on fecal and urinary incontinence from December 10 to 12, 2007.

The purpose of the conference is to assess available scientific evidence about

- the prevalence, incidence, and natural history of fecal and urinary incontinence in the community and long-term care settings
- the burden and impact of this problem on individuals and society
- the risk factors and what can be done to prevent fecal and urinary incontinence
- strategies to improve identifying those at risk and those who have fecal and urinary incontinence
- research priorities in reducing the burden of illness of these diseases

For more information and to register for this conference, go to *www.consensus.nih.gov/2007/2007IncontinenceSOS030main.htm*.

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November 2007