

Urologic Diseases

Research Updates

National Kidney and Urologic Diseases Information Clearinghouse

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NIDDK Advances Collaborative Studies of Urologic Chronic Pelvic Pain Disorders

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), part of the National Institutes of Health (NIH), has launched a research initiative to conduct collaborative studies of urologic chronic pelvic pain disorders by looking for clues outside the bladder and prostate.

Six discovery sites will conduct the studies through the Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network. Two core sites will coordinate data collection, analyze tissue samples, and provide technical support. The total research investment for the 5-year project is estimated to be up to \$37.5 million.

The discovery sites are at

- Northwestern University, Chicago
- the University of California, Los Angeles
- the University of Iowa, Iowa City
- the University of Michigan, Ann Arbor
- the University of Washington, Seattle
- Washington University, St. Louis

Core sites are at the University of Colorado, Denver, and the University of Pennsylvania, Philadelphia.

“The launch of this novel research effort is an excellent example of the NIH’s commitment to encouraging translational research,” said NIH Director Elias A. Zerhouni, M.D. “It also illustrates the NIH’s leadership in furthering innovative approaches to discovering effective new therapies to help our patients.”

The MAPP initiative is unusual in requiring investigators to conduct highly collaborative research of the most common urologic chronic pelvic pain syndromes from a wider systemic perspective. The initiative represents a major shift from earlier organ-specific research on the two most prominent urologic chronic pelvic pain disorders: interstitial cystitis/painful bladder syndrome (IC/PBS) and chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS).

“The MAPP Network’s expanded scientific approach will address many persistent questions about urologic chronic pelvic pain,” said NIDDK Director Griffin P. Rodgers, M.D., M.A.C.P. “Knowing whether there are risk factors common to all the disorders and whether clinical profiles can be identified for each will provide invaluable, fundamental information for developing treatment strategies.”

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The innovative shift in research focus represented by the MAPP initiative is supported by recent epidemiological studies showing that IC/PBS and CP/CPSPS are frequently associated with other chronic pain disorders such as fibromyalgia, chronic fatigue syndrome, and irritable bowel syndrome. These latest findings suggest the possibility of common underlying disease processes in these chronic disorders.

“The bladder was assumed to be the origin of the interstitial cystitis/painful bladder syndrome symptoms and the prostate was assumed to be the source of chronic prostatitis/chronic pelvic pain syndrome symptoms,” explained Leroy M. Nyberg Jr., M.D., Ph.D., the NIDDK urologist heading the program. “However, in spite of intense study funded by the NIDDK, no organ-specific cause has been identified for either disorder.”

New Insights

The MAPP research effort is expected to lead to critical new insights into the underlying causes of urologic chronic pelvic pain. Widening the scope of research will be bolstered by the perspectives of project leaders not normally involved in urologic pelvic pain studies but who have expertise in relevant scientific disciplines. This approach will expand the context in which research into IC/PBS and CP/CPSPS occurs and will encourage a more comprehensive understanding of chronic pelvic pain.

Scientists at discovery sites will conduct individual and collaborative multisite research projects, supported by each core site. An important first step in these studies will be the careful and extensive phenotyping, or clinical characterization, of the men and women participating in the studies.

The data coordination core at the University of Pennsylvania will provide overall administration and coordination of multisite research studies and perform data analyses.

The Tissue Analysis and Technology Core at the University of Colorado will bank,

analyze, and distribute biopsy, serum, and urine samples. Tissue analyses will help in the search for biomarkers, important in screening for diseases and for monitoring treatment outcomes. The core site in Colorado also will perform genomic and proteomic tissue expression analyses, which may lead to new treatment approaches and help predict which patients might respond to these treatments.

In addition to initial collaborative projects by the Network, MAPP investigators will be invited to propose ancillary research projects to further the goals of the collaborative study group. An external Scientific Advisory Committee will review proposals for scientific merit and feasibility.

For more information about the MAPP Research Network, visit www2.nidDK.nih.gov/Research/ScientificAreas/Urology/MAPP. ■

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

Urologic Diseases Research Updates



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, go to <http://catalog.nidDK.nih.gov/newsletter.cfm>. You can read or download a PDF version of the newsletter at www.kidney.nidDK.nih.gov/about/newsletter.htm.

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



Researchers Seek Children for Urinary Tract Disorder Study

Researchers conducting a study to learn if children with a urinary tract disorder known as vesicoureteral reflux (VUR) should receive extended antibiotic treatment seek to enroll more participants. The Randomized Intervention for Children with Vesicoureteral Reflux (RIVUR) study is funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) at the National Institutes of Health.



“The RIVUR study has the potential to help us understand how to provide the best care for thousands of children diagnosed every year with this condition.”

Marva Moxey-Mims, M.D.

Director, Pediatric Nephrology Program, Division of Kidney, Urologic, and Hematologic Diseases, NIDDK

Urine normally flows down to the bladder through tubes called ureters. VUR is the abnormal flow of urine from the bladder back up into the ureters. VUR is the most common functional abnormality of the urinary tract in children. Between 30 to 50 percent of children with urinary tract infections (UTIs) have VUR, which is thought to increase the risk of kidney damage when children have recurring UTIs. At least 30 percent of children who have at least one UTI will have a recurrence.

Researchers seek to enroll 600 participants in the study. Participants must be between the ages of 2 months and 6 years and have had their first UTI within the 16 weeks before their first study visit.

With the approval of 20 institutional review boards and an external data safety monitoring board charged with overseeing the safety of children in the trial, each participant receives a daily dose of an antibiotic or a placebo for up to 2 years. Children who develop recurring fever or other symptoms of infection or scar tissue buildup in the kidneys will be switched from the study to routine antibiotic care and referred to a urologist, depending on the number of infections and degree of renal scarring.

“The RIVUR study has the potential to help us understand how to provide the best care for thousands of children diagnosed every year with this condition,” said Marva Moxey-Mims, M.D.,

director of the NIDDK’s pediatric nephrology program in the Division of Kidney, Urologic, and Hematologic Diseases. “In addition to finding out if antibiotics reduce the risk of UTIs, we also need to understand the progression of renal scarring and the development of resistance to antibiotics in these children.”

Renal scarring occurs between 5 and 40 percent of the time when a child has a UTI. Scarring may accumulate with each infection and can lead to progressive kidney failure and the need for renal replacement therapy, such as dialysis.

About 50 years ago, physicians began to prescribe an ongoing regimen of daily antibiotics for children with VUR, based on the belief that treatment would prevent infection and reduce scarring and kidney failure. Unfortunately, the number of children developing kidney failure from VUR has not changed in that time, leading physicians to question the value of this practice and adding to concerns about increasing antibiotic resistance in the general population.

The National Kidney and Urologic Diseases Information Clearinghouse has more information about VUR at www.kidney.niddk.nih.gov/kudiseases/pubs/vesicoureteralreflux. For more information about the RIVUR study, go to www.clinicaltrials.gov/ct2/show/NCT00405704?term=RIVUR&rank=1. ■

NIDDK Identifies Priorities for Prostate Research

For the first time, a strategic research plan for benign prostate diseases based on the latest scientific knowledge has been published by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), part of the National Institutes of Health. The *NIDDK Prostate Research Strategic Plan* is the culmination of discussions and meetings among experts over the past 2 years in an effort to outline a strategic vision for research into the causes, prevention, and treatment of these elusive and multifaceted diseases.

“The longstanding, unanswered questions about the causes of these disorders prompted the NIDDK to examine the state of the science and develop a new vision for future research.”

Chris Mullins, Ph.D.
Director, Basic Cell
Biology Programs in
Urologic and Kidney
Disease, NIDDK

Research on benign prostate diseases includes two of the most significant noncancerous disorders affecting males—benign prostatic hyperplasia (BPH) and chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS). These conditions are common, chronic, and costly.

BPH, an enlargement of the prostate gland, is often associated with lower urinary tract symptoms (LUTS). LUTS, which can include symptoms such as overactive bladder, restricted or excessive urination, and feelings of urgency, affects men of all races and ethnic groups and can become severe over time. An estimated 50 percent of men in their 50s have BPH, and 26 to 40 percent of men between the ages of 40 and 79 have moderate to severe LUTS.

CP/CPPS is generally described as inflammation of the prostate gland. CP/CPPS is sometimes associated with urinary symptoms, pain, and sexual dysfunction. The source of pain in this syndrome is unknown and there generally are no effective methods for preventing or treating it.

The plan, developed by an expert group of basic scientists, epidemiologists, and clinical researchers, identifies research priorities in four key areas: basic science, epidemiology and population-based studies, translational opportunities, and clinical sciences. Selected recommendations from the plan include the following:

- Promote interdisciplinary research that focuses on how benign prostate diseases are influenced by other organ-specific diseases and systemic conditions, such as obesity, high blood pressure, high cholesterol, cardiovascular disease, diabetes, and erectile dysfunction. For example, the possible influence of high

blood pressure on BPH/LUTS is a previously unexplored area of research.

- Study the primary prevention of benign prostate diseases, including possible benefits of lifestyle changes such as avoidance of alcohol and caffeine, frequency of sexual practice, pelvic massage therapy, stress reduction, and diet modulation for relief of CP/CPPS.
- Develop data and human tissue resources from patients of various ages to derive information useful in investigating risk factors, underlying causes, and natural history of disease progression, quality of life, quality of care, and decision-making regarding benign prostate disease treatment.
- Develop imaging approaches and other biomarker studies to assess severity and risk of progression based on physical and cellular findings.
- Develop targeted medical therapies based on new insights into disease-relevant cellular pathways and physiological events.
- Develop standardized, clinically significant benign prostate disease syndrome definitions and classifications based on measurable phenotypic features.
- Train and mentor epidemiologists, health services researchers, clinical investigators, and students interested in the study of benign prostate disease.

“The longstanding, unanswered questions about the causes of these disorders prompted the NIDDK to examine the state of the science and develop a new vision for future research,” said

Grants Available to Research Impact of Health Communication on Dietary Behavior

The National Institutes of Health (NIH), along with the Centers for Disease Control and Prevention and the U.S. Food and Drug Administration, has issued a funding opportunity announcement (FOA) for research projects focused on creating and executing communication strategies to change dietary behaviors to improve health.

The FOA is designed to promote interdisciplinary research at multiple levels—individual, environmental, and policy—and across diverse populations. Research targeting populations at high risk for obesity, such as children, teenagers, and minority populations, is encouraged.

The funding will be awarded as an R01 and R21 grant. The NIH R01 grant

- supports a discrete, specified, circumscribed research project
- is the NIH's most commonly used grant program
- is not limited to a specific dollar amount unless specified in the FOA
- requires advance permission for \$500,000 or more in direct costs in any year
- is generally awarded for 3 to 5 years

The NIH R21 grant

- encourages new, exploratory, and developmental research projects by supporting the early stages of project development
- is sometimes used for pilot and feasibility studies



- limits funding to 2 years
- usually limits the combined budget for direct costs for the 2-year project period to \$275,000
- generally requires no preliminary data

For complete information about applying for the R01 grant, go to www.grants.nih.gov/grants/guide/pa-files/PA-08-239.html. For more information about the R21 grant, go to www.grants.nih.gov/grants/guide/pa-files/PA-08-240.html. ■

MedlinePlus Health Information Now Available in Multiple Languages

MedlinePlus, a consumer health portal from the National Library of Medicine (NLM), part of the National Institutes of Health, now features reliable health information in many different languages. The collection of health resources contains more than 2,500 links to information in 44 languages covering nearly 250 health topics.



To be included on the MedlinePlus website, the multiple-language information must be produced by the Federal Government or a U.S.-based organization such as a hospital or medical association.

Users can navigate the new collection of health information either by language or topic. The page listing the 44 languages covered in the collection is located at www.nlm.nih.gov/medlineplus/languages/languages.html. The most commonly spoken languages included on the site are Chinese, Korean, Russian, Spanish, and Vietnamese. Links to foreign language information can also be found on individual topic pages, such as the “Urinary Incontinence” topic page at www.nlm.nih.gov/medlineplus/languages/urinaryincontinence.html.

Limited English Proficiency

According to a 2006 survey by the Health Research and Educational Trust of more than 850 hospitals, 80 percent of them treat patients with limited English proficiency. But despite nationwide demand, free, online consumer health information in multiple languages has not been readily available.

To be included on the MedlinePlus website, the multiple-language information must be produced by the Federal Government or a U.S.-based organization such as a hospital or medical association. The information also must be current, authoritative, and appropriate for a U.S. consumer audience.

“As the population of patients and consumers with limited English proficiency increases, more health care providers, patients, and family members will need information in languages from Hindi to Tagalog,” said Paula Kitendaugh, head of the health information products unit in the NLM’s public services division. “By creating a repository of authoritative, free, online information, we hope MedlinePlus will help meet that need.” ■

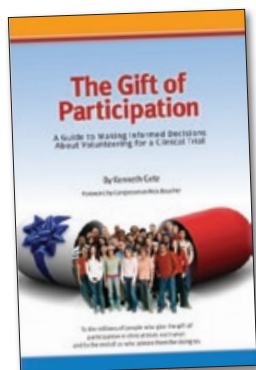
PROSTATE RESEARCH, from page 4

Chris Mullins, Ph.D., the NIDDK’s director of basic cell biology programs in urologic and kidney disease. “As part of this process, we convened the Prostate Research Planning Committee, composed of clinical and basic scientists and epidemiologists from around the country to review and evaluate past and current research and to make individual recommendations for new research priorities. The *NIDDK Prostate Research Strategic Plan* is the result of that collaborative effort.”

The plan is designed to be read by a broad audience of researchers, clinicians, advocacy groups,

representatives of funding organizations, and patients. Each major section includes a mission statement, lay summary, overview of current knowledge, and high-priority recommendations for future research.

For a complete copy of the *NIDDK Prostate Research Strategic Plan*, visit the NIDDK website at www.niddk.nih.gov. To buy a copy in print or compact disc format for \$1, go to www.catalog.niddk.nih.gov/PubType.cfm?Type=182&CH=NKUDIC. The NIDDK has a fact sheet about BPH at www.kidney.niddk.nih.gov/kudiseases/pubs/prostateenlargement. ■



Featured in the NIDDK Reference Collection

Clinical Trials

The Gift of Participation: A Guide to Making Informed Decisions About Volunteering for a Clinical Trial describes why clinical trials are conducted, why people choose to participate in them, the importance of becoming educated about clinical trials, how to locate an appropriate clinical trial, the concept of informed consent, clinical trial care and compensation, the role of institutional review boards, historical events that have shaped human subject protection, considerations for special populations, and what to do when things go wrong. The book also has nine appendices that include a glossary and a history of key regulations and guidelines affecting patient protection in clinical research. The book's author, Ken Getz, is the founder of the Center for Information and Study on Clinical Research Participation, which provides outreach and education to people who are considering joining a clinical trial. The 360-page book is available for \$19 at the center's website, www.ciscrp.org/e-store/books.asp.

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. The NIDDK does not control or endorse the information contained in this collection; the information is provided as a convenience to our visitors. To find resources about urologic diseases, visit www.catalog.nidk.nih.gov/resources. ■

Additional Resources

Interstitial Cystitis/Painful Bladder Syndrome

People with interstitial cystitis/painful bladder syndrome (IC/PBS) usually have pain when the bladder fills and empties. Although the pain might disappear for weeks or even months, it then returns. Finding a proper diagnosis for IC/PBS can be frustrating because symptoms can resemble those of other conditions.

An easy-to-read booklet from the National Kidney and Urologic Diseases Information Clearinghouse (NKUDIC) helps people understand the difference between IC/PBS and other sources of bladder pain. *What I need to know about Interstitial Cystitis/Painful Bladder Syndrome* explains the tests and treatments for IC/PBS, including bladder retraining, physical

therapy, physical activity, stress reduction, medication, bladder stretching, nerve stimulation, and surgery. The booklet is available at www.kidney.nidk.nih.gov/kudiseases/pubs/interstitialcystitis_ez.

Children and Urinary Tract Infections

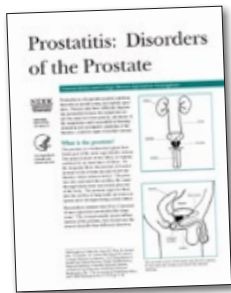
Urinary tract infections (UTIs) affect about 3 percent of children in the United States annually. Throughout childhood, the risk of having a UTI is 2 percent for boys and 8 percent for girls. UTIs account for more than 1 million visits to pediatricians' offices each year.

A booklet from the NKUDIC explains the symptoms of UTIs, how doctors diagnose and treat them, and how to prevent them. Symptoms of UTIs are not always obvious to parents, and younger children are usually unable to



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describe how they feel. However, recognizing and treating UTIs are important because lack of treatment can lead to serious and even life-threatening kidney problems. *What I need to know about My Child's Urinary Tract Infection*, an easy-to-read publication, is available at www.kidney.niddk.nih.gov/kudiseases/pubs/utichildren_ez.



Prostatitis

Prostatitis: Disorders of the Prostate describes the four types of prostatitis: acute bacterial prostatitis, chronic bacterial prostatitis, chronic prostatitis/chronic pelvic pain syndrome, and asymptomatic inflammatory prostatitis. Prostatitis, or inflammation of the prostate, is an often painful condition that affects mostly young and middle-aged men. Symptoms—which include painful or burning urination and incomplete bladder emptying—can vary or mimic signs of other illnesses, making diagnosis difficult. This NKUDIC fact sheet also explains how doctors diagnose and treat prostatitis. For a copy of the fact sheet, go to www.kidney.niddk.nih.gov/kudiseases/pubs/prostatitis.

New Interactive Tools

New to the Interactive Health Education Tools section of the National Institute of Diabetes and Digestive and Kidney Diseases website is

Streaming Audio

- Researchers Seeking Children for a Urinary Tract Disorder Study



The website's interactive tools section consolidates all the tools and resources about urologic diseases from the National Institutes of Health and the National Library of Medicine. To access these resources, visit www.kidney.niddk.nih.gov/resources/HealthTools. ■

Upcoming Meetings, Workshops, and Conferences

Urinary Incontinence

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) will sponsor a meeting titled "NIDDK New Research Directions in Urinary Incontinence Symposium" on January 7–9, 2009, in Bethesda, MD.

The intent of the meeting is to gather new concepts and directions for research and treatment

of urinary incontinence in men and women. The agenda includes an active poster session, lectures, and roundtable discussions. For more information and to register for the meeting, go to www3.niddk.nih.gov/fund/other/incontinence. ■