



HOPE FOR UNDERSTANDING PROSTATE CANCER AND DEVELOPING BETTER TREATMENTS



DAVID JARRARD, MD
PROFESSOR

Bench to Bedside: The Wisconsin Institutes for Medical Research (WIMR), adjacent to UW Carbone Cancer Center, is home to many research programs including the prostate cancer research lab of Dr. David Jarrard. The proximity of WIMR to patients speeds the transfer of treatment options to those who will benefit from them.

Research in the University of Wisconsin Department of Urology is unraveling the mystery of why aging men often develop prostate cancer, the most commonly found cancer in men.

One frequent finding is inflammation in the prostate. Work performed by Dr. Travis Jerde, a post-doctoral fellow in Dr. Wade Bushman's lab, was recently accepted for publication in the prestigious journal *Science Signaling* and will be featured on the journal's cover. This work shows that the molecular signaling pathways involved in inflammation actually play a role in normal prostate development. The implication of this finding is summarized by the editor

and an accompanying commentary. "Noting that both inflammation and reactivation of developmental signaling pathways are associated with adenocarcinomas—another condition associated with epithelial and progenitor cell proliferation and stromal remodeling—the authors speculate that inflammatory mediators may play a conserved role in promoting epithelial proliferation in all of these conditions." These important findings will lead to the development of better treatments to prevent prostate cancer and may help explain why some anti-inflammatory medicines, such as aspirin, have a role in cancer prevention.

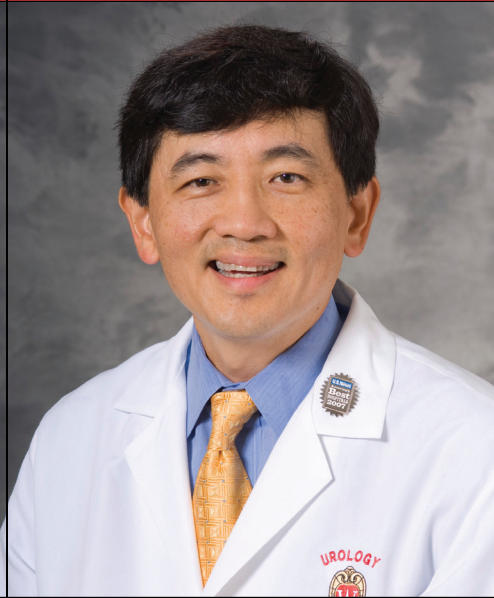
In a second study, researchers pinpointed a gene behavior that

could mark susceptibility to prostate cancer. The findings were published in a recent edition of *Cancer Research*. Dr. David Jarrard, principal investigator and urologist at the UW Carbone Cancer Center, says the findings may give us a window into preventing prostate cancer in aging men, as well as a mechanism to diagnose the disease in early stages.

Dr. Jarrard and his research team found an erosion of normal gene regulation, or imprinting, that encourages a cancer promoter linked to the development of prostate cancer. Researchers then examined normal-appearing prostate tissues in aging men and found that this same alteration occurred more commonly in men who developed associated cancer. "We are setting up a trial to look at this gene change as a marker for men who develop cancer in a broader group of patients both within and outside UW," Dr. Jarrard explains.

Another important thrust of ongoing work is determining whether this aberrant gene behavior can be prevented or slowed through dietary additions. Both of these studies shed light on the development of prostate cancer that will assist in our efforts to control the disease. **WU**

>> A MESSAGE FROM THE CHAIR



STEPHEN Y. NAKADA, MD

The watchword these days is quality. In the midst of significant healthcare reform, and an ongoing economic recovery, quality of care, cure of disease and hope reign supreme in these times.

With that being said, I am happy to announce that the department had an excellent year from a clinical and

a research standpoint in spite of all the prevailing national and global difficulties. Moreover, I am most delighted that this year we achieved our highest ranking ever in *US News and World Report*, twenty-sixth in the survey. Urology was one of only five specialties from UW ranked.

This year we said goodbye to Dr. Reg Bruskewitz who served the Department of Urology for 30 years. Reg will be sorely missed by clinical faculty, clinical staff, research staff, residents and most importantly, his patients. We wish him well in his retirement. Dr. Jason Gee is also moving on after six great years with us in Madison. Dr. Gee is relocating to the Lahey Clinic in Burlington, Mass. We wish him the very best.

This fall is rich with lectures and meetings in our department. We are happy to host the first annual Robert F. Schnoes Lecture Series. The first Schnoes Lecturer will be Dr. Donald Coffey from Johns Hopkins University. The lecture is scheduled to take place on October 22, 2009. The following month will bring the 2009 Uehling Lectures. We are thrilled to have Dr. Anthony Atala, Professor and Chairman from Wake Forest

University on November 6, 2009. Dr. Atala is a highly touted world authority in regenerative medicine, and he will speak on his research as well as give an update in pediatric urology.

Deanna and I are also very excited to host the upcoming North Central Section Meeting in Scottsdale, Ariz. The meeting will be held November 9-14, 2009, and we have the opportunity and privilege to honor Dr. David Uehling at this annual meeting. Dr. Reg Bruskewitz will introduce Dr. Uehling and there will be many great speakers including Drs. Margaret Pearle, Glenn Preminger, Ray Leveillee, Dean Assimos and Ron Rabinowitz.

I hope you have an enjoyable fall. We look forward to seeing you at the Robert F. Schnoes Lecture Series, the Uehling Lectures and the upcoming North Central Section Meeting in Scottsdale! **WU**

STEPHEN Y. NAKADA, MD
CHAIRMAN AND THE UEHLING
PROFESSOR OF UROLOGY

>> UPCOMING WISCONSIN EVENTS TRICIA MAIER

• Uehling Lectures

Please mark your calendars for this yearly event!

2009 Uehling Lectures

The University of Wisconsin Department of Urology will hold its annual David T. Uehling Lectures on **Friday, November 6, 2009**, at the Fluno Center in Madison, Wisc. This year the title of the Uehling Lecture Series is "State of the Art Regenerative Medicine and Update in Pediatric Urology." Lecture topics will encompass diagnosis and management of hydronephrosis, continent diversion in children and regenerative medicine. **Our keynote speaker is Anthony Atala, MD, Professor and Chair, Department of Urology at Wake Forest University School of Medicine in Winston-Salem, North Carolina.**

Dr. Atala is the Director of the Institute for Regenerative Medicine at Wake Forest University. His clinical interests include pediatric and adolescent urology, microsurgery, and reconstructive urology

with research interests in regenerative medicine and reconstructive urology. **Please be sure to join us in November!** Brochure and registration materials will be coming soon.

• Future Uehling Lectures at the Fluno Center

2010 Uehling Lectures

The 2010 Uehling Lectures are scheduled for **Friday, October 29, 2010**. Our keynote speaker is William D. Steers, MD, Hovey Dabney Professor of Urology and Chair of the Department of Urology at the University of Virginia, School of Medicine. Dr. Steers' clinical interests include voiding and sexual dysfunction, prostate disease and robotic surgery.

• Department Visiting Professors

2009 Robert F. Schnoes Lecture Series

October 22, 2009
DONALD S. COFFEY, PhD

The department will be holding the first annual Robert F. Schnoes Lecture Series

this fall. We have invited Dr. Donald Coffey who will give a lecture titled "Why Are We Having Such Difficulties In Preventing and Treating Human Cancers and What Might Help: A 50-Year Point of View." Donald S. Coffey, PhD, is a Professor of Urology, Oncology, and Pharmacology and Molecular Sciences at the Johns Hopkins University School of Medicine. He is Director of the Research Laboratories of the Department of Urology. A prominent urological scientist, Dr. Coffey was appointed as the Catherine Iola and J. Smith Michael Distinguished Professor of Urology at the Johns Hopkins School of Medicine. Dr. Coffey has received many awards during his distinguished career including the Fuller Award from the American Urological Association and the First Society of International Urology-Yamanouchi Research Award. He is also the recipient of two Merit Awards from the National Institutes of Health and has published over 200 research papers. **WU**

Minimally Invasive Options Are Changing the Management of Ureteral Reflux at AFCH

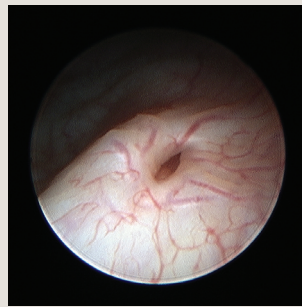
JOHN V. KRYGER, MD, FAAP - ASSOCIATE PROFESSOR



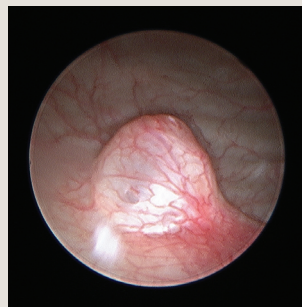
Exciting new options and paradigms are now shaking previously traditional views on the management of vesicoureteral reflux (VUR) at American Family Children's Hospital (AFCH).

Drs. Bruce Slaughenhoupt and John Kryger have contributed their findings to national studies improving the care of children afflicted with VUR. Essentially, VUR occurs when an abnormal check-valve in the bladder allows urine to back up into the kidney. This allows bacteria in the urine to flow freely up into the kidney from the bladder. It is not uncommon for bacteria to colonize the urine, especially in girls. Usually these bacteria would be cleared by normal urinating. But in the presence of reflux, they flow directly into the kidney and increase the risk of kidney infection. Kidney infections are a direct cause of inflammation, scarring, permanent kidney damage and hypertension.

A reprieve from the distress of invasive X-rays and daily antibiotics is in the works. A minimally invasive approach has achieved widespread popularity as a treatment choice by pediatric urologists. Newer injectable materials, coupled with improved techniques of injection and endoscopic technology, have improved success, durability, and safety of the technique. Patients benefit from an earlier withdrawal from antibiotic prophylaxis and fewer X-rays.



PRE-DEFLUX



POST-DEFLUX

Endoscopic injection for treatment of VUR with dextranomer/hyaluronic acid (Dx/HA)(Deflux®) was FDA approved in 2001 for the treatment of Grade II to IV ureteral reflux. In some ways it is similar to injecting collagen to puff up one's lips. It is a relatively brief outpatient surgical procedure. However, over the years, it has been applied to more complex circumstances such as severe reflux, duplicated ureters, ectopic ureters, and previously reimplanted ureters. Other injectable materials have also been studied at the UW, such as calcium hydroxyapatite (Coaptite®), which has not received final FDA approval in the United States.

Cure rates of 80 to 90% have been achieved at AFCH. Higher success rates are demonstrated among pediatric urologists who have performed at least 20 procedures. It is also very important that the treating physician addresses the proper diagnosis and therapy for concomitant voiding dysfunction. When these issues are not properly addressed, there is also potential

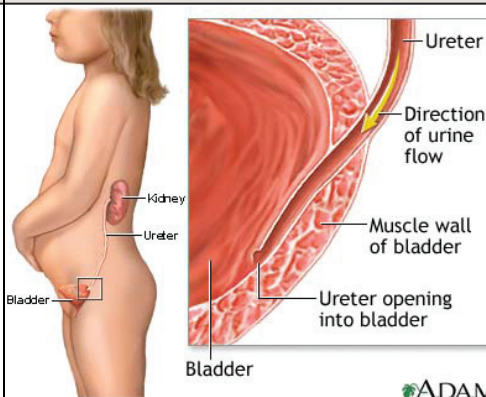
for higher incidence of recurrent urinary tract infections (UTI) and treatment failures.

Studies of the long-term success are limited. Among patients who achieved initial success, follow-up VCUGs performed 2 to 5 years later demonstrate approximately 90 % remained cured. Those patients that continue to reflux after initial therapy or who experience relapse have been corrected by a repeat injection or subsequent ureteral reimplantation. Ureteral reimplantation after failed endoscopic injection may be technically more demanding.

Dx/HA is slowly biodegradable and raises concern of durability and possible recurrent VUR. The consequences of recurrent refluxers presenting at older ages is unknown. Furthermore, many of these patients may be lost to follow-up with the presumption that they were cured of any reflux as a child. One would presume the greatest risk for this would occur among patients with severe reflux.

Another concern is possible overtreatment of children with reflux who may not require intervention for their VUR or may otherwise resolve spontaneously. There is enticement to undergo injection therapy as a substitution for antibiotic prophylaxis and there are long-term studies that support conservative management of VUR, even without preventative antibiotics. One must not completely disregard the lessons learned from the past.

Endoscopic therapy certainly has a place in the algorithm of VUR treatment. However, future studies must continue to carefully assess outcomes. It must also be applied judiciously to properly selected patients and performed by practitioners with a thorough knowledge of these issues and adequate training in the technique. **WU**



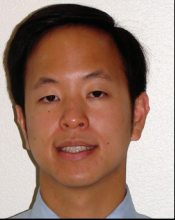
ADAM

Vesicoureteral Reflux image. 16 May 2007. HowStuffWorks.com (<http://healthguide.howstuffworks.com/vesicoureteral-reflux-picture-a.html>). 17 September 2009.

>> RESIDENCY UPDATE

2009-2010 FIRST-YEAR RESIDENTS

NANCY HAWKINS



**KELVIN WONG,
MD**

Dr. Wong received his medical degree from the University of Toledo College of Medicine in Ohio. He completed his undergraduate education at Cornell University in Ithaca, New York. Dr. Wong was a member of Alpha Omega Alpha and a student member of the American College of Surgeons. Most recently, he worked with Dr. Steven Selman at the University of Toledo on a research assignment evaluating the effects of EGCG (green tea compound) on 5- and 12-lipoxygenase expression in T24 human bladder cancer cell lines. He was President of the Surgery Club at the University of Toledo overseeing and arranging club events, fundraising for the Arthritis Foundation, promoting interest in surgery through panels and lectures, and helping first-year students by hosting a mock practical anatomy session. His hobbies include running, tennis, medical missions, basketball and video games.



**AARON
POTRETZKE,
MD**

Dr. Potretzke received his undergraduate degree from the University of Minnesota in Minneapolis and then went on to earn his medical degree from the University of Minnesota Medical School. Dr. Potretzke was elected to the Arnold P. Gold Humanism

Honor Society by his peers in 2008. He has received scholarships from the Minnesota Medical Foundation and the Lyle Korum Foundation. In 2006 he received a student research grant from the Minnesota Medical Foundation. He researched and co-authored a review article on the topic of imaging in the diagnosis and management of urolithiasis which was published in *Current Opinions in Urology*. He has volunteered as a CATALYST Volunteer, Healthcare Student Coordinator, Admissions Ambassador, Board of Trustees Student Representative and Delegate and Chairperson of Community Service for the American Medical Association. His hobbies include music, softball, golf, hunting and running. **WU**

>> NOTABLE AND NEWSWORTHY

• **University of Wisconsin Hospital and Clinics was ranked twenty-sixth in urology** by *U.S. News & World Report* in its August 2009 "America's Best Hospitals" issue.

• Congratulations to **Dr. Wade Bushman!** He received a \$60,000 grant from the NIH to perform pilot studies on the effect of diabetes on the prostate.

• **Dr. John Kryger** is serving a one-year term as president of the Wisconsin Urological Society.

• **Dr. David Jarrard** is serving a one-year term as president of the Society for Basic Urologic Research. He is only the third physician to lead the society in its 23-year history.

• The Society for Male Reproduction and Urology (SMRU) recognized **Dr. Daniel Williams and resident Dr. Josiah Nelson** for presenting the prize paper "The Use of Biased Language and Inaccurate Information about Male Factor Infertility on Fertility Clinic Websites in the United States," at its annual meeting.

• Work performed by **Travis Jerde, PhD**, a post-doctoral fellow working

under Dr. Wade Bushman, was just accepted for publication in the prestigious journal *Science Signaling* and will be featured on the journal's cover. This work shows that the molecular signaling pathways involved in inflammation actually play a role in normal prostate development.

• ABCnews.com featured **Dr. Daniel Williams** on the Health section of its Web site in an article titled "Avoid or Ignore?: Eleven Sperm-Killing Suspects."

• Work performed by **Aubie Shaw, PhD**, when she was a graduate student in Dr. Bushman's lab was accepted for publication in the journal *Oncogene*. This paper describes the activity of Sonic Hedgehog signaling in prostate cancer and identifies a specific gene expression fingerprint of hedgehog signaling that identifies those tumors in which hedgehog signaling promotes tumor growth.

• UW medical student **Ian McLaren** is working with **Dr. Stephen Nakada** and **Kristina Penniston, PhD**, to examine the epidemiology of kidney stones in northern Wisconsin as part of the Shapiro Summer Research Program. The project is a collaboration with the Marshfield Clinic Research Foundation through the UW Institute for Clinical and Translational Research (ICTR).

• A big welcome to **Lindsay Wilkinson, PA-C**, who joined the One South Park Street Urology Clinic on July 13th. Lindsay graduated from the PA Program at the UW School of Medicine and Public Health after earning a Bachelor of Science degree in Chemistry and Biology from Edgewood College.

• **Dr. Jason Gee** left the Department August 5th to join the Lahey Clinic in Burlington, Mass. Good luck Dr. Gee!

• Chancellor Carolyn "Biddy" Martin has conferred emeritus status on **Dr. Reginald Bruskevitz** who retired in June. Congratulations Dr. Bruskevitz! **WU**



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