Possible benefits of green tea polyphenols for prostate cancer
Providing new hope for children with voiding dysfunction
A case of chronic pelvic pain syndrome
A New Model of Care and Discovery

Welcome to the premier issue of *UH Innovations in Urology*. In these pages we introduce some of our outstanding clinicians and scientists in the University Hospitals Urology Institute who are creating a new model of care and discovery for urological diseases.

Our new model of care relies on two elements. First, the formation of multidisciplinary teams of clinicians who work together seamlessly to provide clinical care, perform clinical and translational research, and educate the next generation of clinicians. Because this model focuses on facilitating care for our patients, we have named our clinics from their perspective—“Prostate Cancer” and “Pelvic Pain,” for example—rather than by using traditional “ology” nomenclature, such as urology or gynecology.

In our cover story, we feature our Female Pelvic Medicine & Surgery Center in which urology and gynecology surgeons and physical therapists are fully integrated (administratively, clinically and financially), providing one-stop care for patients with female pelvic floor disorders, such as urinary incontinence and pelvic organ prolapse.

In other articles, we present our Pelvic Pain Center and highlight our new Pediatric Urology Center. The Pelvic Pain Clinic includes urologists, gynecologists, neurologists, family physicians, pain anesthesiologists and psychologists who provide complete care for patients with pelvic pain manifestation caused by interstitial cystitis, chronic prostatitis, vulvodynia, fibromyalgia and other related conditions all in one clinic.

The second element of our new model of discovery relates to seamless, daily transformation of clinical questions into research projects. Our surgeon-scientists and scientists have adopted an infrastructure and mindset that includes daily conceptualization of clinical or translational research projects that are then implemented into clinical or laboratory studies. Promising data from this robust process are analyzed and prepared for formal research proposals or published with the assistance of full-time biostatisticians, clinical epidemiologists, and publication team members. In this issue, we highlight one such research investigation involving the promising effects of green tea extracts on prostate cancer.

We hope you enjoy this first issue of *UH Innovations in Urology* and welcome your comments, questions and suggestions.

Warm Regards,

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Among the nation’s leading academic medical centers, University Hospitals Case Medical Center is the primary affiliate of Case Western Reserve University School of Medicine, a nationally recognized leader in medical research and education.

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The commitment to exceptional patient care begins with revolutionary discovery. Faculty at the Case Western Reserve University School of Medicine, who also are physicians at UH Case Medical Center, are at the forefront of medical research and innovation. The School of Medicine is the largest medical research institution in Ohio and among the nation’s top medical schools for research funding from the National Institutes of Health.
Green Tea Polyphenols for Prevention of Prostate Cancer
An alternative to ‘watchful waiting’ in early stages of disease

Currently, no viable treatment options involving suppression of cancer progression are available to patients with newly diagnosed prostate cancer. During the earliest stages of the disease, many individuals and their clinicians elect to engage in either “watchful waiting” or “active surveillance”; these strategies involve deferring treatment and carefully monitoring clinical findings and serum PSA at regular intervals. Although the cancer may advance very slowly, currently there are no options that would allow changing the course of the disease.

Sanjay Gupta, PhD, Carter Kissell Associate Professor and Research Director, Department of Urology, Case Western Reserve University School of Medicine, is engaged in furthering research into the efficacy of green tea polyphenols in suppressing the onset of invasive prostate cancer.

In a 2006 pilot study, Bettuzzi et al. found that green tea polyphenol was effective in reducing the risk of occurrence of invasive prostate cancer. Only 3 percent of men (1 of 30) with high-grade prostate intra-epithelial neoplasia (a putative precursor of invasive prostate cancer) receiving daily capsules of green tea catechins developed invasive prostate cancer within one year, as compared with a 30 percent incidence of invasive cancer in men (9 of 30) who received a placebo capsule during the same period.

The study was unique in that early stage cancer patients were recruited rather than those with advanced disease. Dr. Gupta explains that green tea polyphenols may cause PSA reduction in individuals with advanced disease but that eventually the reduction is overcome by the disease burden.

High-Fat Diet and Prostate Disease
Sanjay Gupta, PhD, and colleagues at the Urology Institute of University Hospitals Case Medical Center also are researching the deleterious effects of a high-fat diet on the prostate. In a study recently accepted in the journal The Prostate, Dr. Gupta’s group demonstrated that a high-fat diet results in activation of nuclear factor kappa B – a protein complex that controls DNA transcription that is activated as a result of inflammation and stress – in the abdominal cavity, thymus, spleen and prostate. Compared with mice fed a regular diet, a high-fat diet group had significant increases in prostate weight, and in the prostate expression of markers of oxidative stress and inflammation. This research provides direct evidence that a high-fat diet can lead to benign prostatic hyperplasia, prostatitis and cancer of the prostate.

PHASE 2B RESEARCH AT UNIVERSITY HOSPITALS UROLOGY INSTITUTE
In collaboration with colleagues at University Hospitals Case Medical Center, Dr. Gupta’s Phase 2b study recently began recruiting men with early stage, clinically localized T-1 and T-2 stage prostate cancers to assess the therapeutic efficacy of green tea polyphenols in the prevention and treatment of prostate cancer. The research also will investigate new biomarkers that may help define disease progression, in addition to PSA.

Patients enrolled in the trial will receive green tea polyphenol capsules for six weeks before radical prostatectomy. During the treatment phase, blood samples will be evaluated for PSA levels as well as several other potential biomarkers. Following surgery, excised prostate tissue will be histochemically analyzed for concentrations of biomarkers and polyphenol levels. “The bio-distribution of polyphenols in various tissues is very different and is very important in analyzing their potential role in the management of prostate cancer,” explains Dr. Gupta.

Despite attempts at definitive curative therapy with surgery and/or radiotherapy in patients with clinically localized disease, prostate cancer recurs in about 30 percent of cases. Currently, there are no viable therapeutic strategies aimed at preventing such recurrences after initial potentially curative treatments. Based on the work of Dr. Gupta and his colleagues, the UH Urology Institute’s Disease Prevention Center will offer patients participation in studies and counseling on effective lifestyle modification, including nutritional and dietary regimens and chemoprevention for prevention of prostate cancer and other urological diseases.

Enrolling Patients
The phase 2b clinical study in patients with T-1 and T-2 prostate cancer is now enrolling patients. For more information please contact Claudia Lillibridge, CMA, CCRP, Clinical Research Coordinator, UH Urology Institute, at 216-844-8205 or Claudia.Lillibridge@UHhospitals.org.
Launching a New Model of Care in Female Pelvic Medicine & Surgery

University Hospitals Urology Institute adopts an effective integrated multidisciplinary approach

The new University Hospitals Urology Institute’s Female Pelvic Medicine & Surgery Center is home to a multidisciplinary team committed to utilizing advanced technology and a fully integrated approach to address Female Pelvic Floor Disorders (FPFD). The Center’s unique approach brings together experts that include urologists, urogynecologists, nurse practitioners, urodynamic technicians, colorectal surgeons, pelvic floor physical therapists and psychologists.

FPFD, such as urinary incontinence and pelvic organ prolapse, impact an individual’s quality of life but are often overlooked because of the associated stigma and the erroneous belief that this development is a normal part of aging. Women also may find it difficult to know which kind of specialist can be most effective in providing treatment – a gynecologist or a urologist.

The Center is not a virtual gathering of urological and gynecological surgeons. Rather, it is a group of colleagues who work side by side and who each bring a unique skill set to focus on women’s pelvic floor concerns. “We are visionary in that we are looking to the future and looking to complement each other in our expertise in order to maximize patient quality of care,” says Sangeeta Mahajan, MD, urogynecologist and Director of the Fellowship Program in Female Pelvic Medicine/Reconstructive Surgery, UH Urology Institute, and Assistant Professor, Case Western Reserve University School of Medicine.

UNDER ONE ROOF
In most institutions throughout the United States, surgeons who treat FPFD are housed in separate facilities according to their traditional specialties. In contrast, at the UH Urology Institute’s Female Pelvic Medicine & Surgery Center, team members are not only professionally integrated, but they also see patients in a combined clinic, making such integration a reality, notes Adonis Hijaz, MD, Director of the Center for Female Pelvic Medicine & Surgery, UH Urology Institute, and Associate Professor, Case Western Reserve University School of Medicine.

The close physical proximity of the surgeons under one roof benefits the patients as well as the surgeons. In any setting, it is not uncommon for a clinician to seek out a colleague for a unique perspective about a challenging case. At the Female Pelvic Medicine & Surgery Center, this interaction takes place every day and is evident in the individualized delivery of care.

An important premise of the Center is that various female pelvic floor issues coexist. Patients who have urinary incontinence often have rectal prolapse, fecal...
incontinence or vaginal prolapse. Female pelvic surgeons at the Center evaluate these issues simultaneously so that patients are not required to see a gynecologist for the prolapse, a urologist for the incontinence, and a colorectal surgeon for the fecal incontinence. Additionally, due to the expertise of the Center’s surgeons multiple issues potentially can be addressed during one surgical approach, benefiting patients and improving outcomes.

**COMPREHENSIVE AND INDIVIDUALIZED CARE OPTIONS**

In treating patients, surgeons at the Female Pelvic Medicine & Surgery Center incorporate lifestyle changes, physical therapy and medications when possible. If surgery becomes necessary, the Center’s physicians offer expertise in robotic and laparoscopic surgical procedures. With robotic techniques, a surgeon is able to conduct an operation with the same steps used in a traditional open procedure, except using smaller incisions.

The human hand/wrist has 12 degrees of freedom, or movements, but this is limited to only four to six degrees of freedom during laparoscopic surgery. Therefore, laparoscopic surgery requires additional steps and adaptations to accommodate this limitation.

The robot allows 12 degrees of freedom, as with the human hand, so the same surgical steps that are used in traditional surgery are possible using the robot. In pelvic surgery, robotics is a particularly useful tool in sacral colpopexy, in which the top of the vagina is suspended to the sacrum using a mesh graft. A traditional 10-cm incision can be translated to five 1-cm incisions. The resulting reduced facial plane facilitates healing and reduces the patient’s time to recovery from six weeks to two weeks on average. Surgeons at the Center are experienced in additional robotic-assisted surgical procedures, including: sacrocolpopexy, colpopoeisis, and advanced fistulas and hysterectomy.

**EDUCATIONAL OPPORTUNITIES**

The integrated, multidisciplinary approach at the Female Pelvic Medicine & Surgery Center not only enriches clinical practice but an additional benefit is that it also provides an excellent opportunity for residents and fellows. They participate in weekly meetings to discuss the literature, clinic cases and research, and develop expertise with cutting-edge techniques, such as robotically assisted surgery and the use of botulinum toxin. The Center has begun offering a fellowship certified by the American Board of Obstetrics and Gynecology that will be awarded to either a gynecologist or a urologist to focus on treating women’s pelvic health concerns. The training program will include rotations, lectures and a strong research focus. Immersing new surgeons in the multidisciplinary approach at the Center will promote the beneficial practice of treating FPFD as a whole.

**The Power of Integration**

The Center includes fellowship-trained physicians in female urology, urogynecology and colorectal surgery. These physicians are complemented by a support staff of three nurse practitioners, three urodynamic technicians and four physical therapists.

Physician team members of the UH Urology Institute’s Female Pelvic Medicine & Surgery Center are: Sam Ahuja, MD; Firouz Daneshgari, MD; Adonis Hijaz, MD; Sangeeta Mahajan, MD; Tatiana Sanses, MD; Joseph Shawi, MD; and Sharon Stein, MD.

**Offer Your Patients a Solution**

Patient referrals can be scheduled by calling 1-866-UH4-CARE, or to speak with one of the specialists from the Female Pelvic Medicine & Surgery Center regarding a patient consultation, please call 216-844-3661.
Since joining University Hospitals in 2009, Jonathan Ross, MD, has been involved in developing groundbreaking minimally invasive surgery and planning a comprehensive voiding dysfunction clinic. Dr. Ross – a leading regional and national expert in pediatric urology – is Director, Pediatric Urology at University Hospitals Urology Institute, and Division Chief, UH Rainbow Babies & Children’s Hospital and Professor of Surgery, Case Western Reserve University School of Medicine.

Dr. Ross and his colleague, Edward Cherullo, MD, were among the first to employ laparoendoscopic single site (LESS) techniques, rather than traditional methods, to perform nephrectomies in children. Unlike traditional laparoscopic nephrectomies, in which several incision sites are used to insert telescopes and tools for kidney removal, LESS nephrectomies involve one incision site near the navel and access via a multiper device.

The advantage is even greater when conducting bilateral nephrectomies, in which multiple access sites are typically necessary. For their series of operations, Drs. Ross and Cherullo performed one unilateral and two bilateral complete nephrectomies. A full report on this cutting-edge work will be published in an upcoming issue of the Journal of Endourology.

In more complex cases, extensive evaluation using state-of-the-art urodynamics and radiographic studies will be utilized.

A NEW CLINIC
Dr. Ross is building a comprehensive voiding dysfunction clinic as part of the new Pediatric Urology Center of Excellence at University Hospitals. “We have the ability to employ a full range of treatment,” he says, “including a thorough evaluation, behavioral and medication therapies, and more advanced procedures such as neuromodulation and Botox injection.”

The noninvasive techniques of ultrasonography and uroflow/ electromyogram (EMG) will be available. In more complex cases, extensive evaluation using state-of-the-art urodynamics and radiographic studies will be utilized. The clinic will include a multidisciplinary team from pediatric urology, pediatric behavioral psychology and pediatric gastroenterology, which will allow an integrated patient management strategy.

Children who will benefit from the voiding dysfunction clinic include those with common nighttime and daytime wetting problems, those with urgency symptoms (overactive bladder), and those with more severe problems, such as neurogenic bladder related to spina bifida. If surgery becomes necessary, patients and their parents can be assured that it will be performed by experienced urologists who are well-versed in advanced approaches, such as the latest sling techniques and artificial sphincters.

The clinic also will be a source for prospective data collection and will allow patients to participate in studies of innovative approaches to voiding problems. Ongoing research involves collaboration with the biomedical engineering department to develop modalities for modifying the interactions between the nerves and the bladder.

OFFERING SOLUTIONS
The clinic will give hope to many children who currently are not adequately treated, which occurs for a variety of reasons. Oftentimes, the problem may seem too difficult to treat. Pediatric patients and their parents may be frustrated after initial attempts to solve a voiding dysfunction have failed. Or parents may not realize how serious the problem is. Moreover, their child may minimize the situation because of embarrassment. “There is an underappreciation of the psychosocial impact for the child,” notes Dr. Ross.

Primary care physicians and urologists should consider eliciting these problems during routine evaluations. Dr. Ross sees the UH Urology Institute’s Center for Pediatric Urology as a truly comprehensive program that provides thorough evaluations and employs a full range of multidisciplinary treatments tailored to the child and his or her family.
A 41-year-old man presented to the Pelvic Pain Center at University Hospitals Case Medical Center with a seven-year history of intermittent, dull, perineal pain and intermittent testicular pain. He had been treated empirically with antibiotic, after which the pain improved gradually. He was afebrile throughout all previous pain episodes and had never had a positive urine culture.

Following a symptom-free period, the pain recurred, which coincided with a new job and career change. Among these most recent symptoms, he now was experiencing some urinary frequency and bowel changes, including pressure and urgency, with some relief of the pressure sensation after a bowel movement. The new job involved longer periods of sitting, driving and traveling. His exercise program was inconsistent, although he maintained a healthy diet. The pain symptoms had led to decreased sexual desire and subsatisfactory erections.

EVALUATION
The patient was examined by Jeannette Potts, MD, at the University Hospitals Urology Institute’s Pelvic Pain Center. He was afebrile; his urinalysis was normal.

Remarkable findings on physical exam included abdominal wall tenderness and marked pain on palpation of the rectus muscle insertion sites over the pubis. The adductor muscles were likewise tender at the proximal insertions and up to midway down the medial thigh, right worse than left. The perineum was tender on exam, including the ischial tuberosities. Genitals were normal, though his right testicle was sensitive. The internal pelvic floor exam confirmed presence of coccygodynia. The levator ani muscles were abnormal; taut bands were palpable, especially on the right side. Provocative testing of the obturator internus muscles demonstrated weakness and pain on the right side. The prostate gland was normal in texture; sensitivity was appropriate.

TREATMENT
Dr. Potts explained her findings to the patient and validated his pain. Lack of success in the past had led previous specialists to conclude the pain was psychosomatic, so validation was important. She used diagrams and anatomical models to explain the pathophysiology of myofascial pain and related trigger points that can relay pain in a distributed, predictable pattern. Three goals for successful treatment were set: to decrease (1) the intensity, (2) the frequency and (3) the duration of the pain flare-ups. The patient was prescribed a regimen of specific physical therapy, which was initiated at the Pelvic Pain Center and continued with a physical therapist nearer to the patient’s home. This form of specialized physical therapy involves education, pelvic floor relaxation techniques and biofeedback. Often, external and/or internal myofascial trigger point release is performed through manual or digital techniques. A self-care regimen is paramount to success and includes daily exercise and stretching regimens tailored to the patient’s postural, athletic or occupational needs. This was started concurrently and continued after physical therapy.

Education, empowerment and self-care are the cornerstones to successful management and therapy. After three months, the patient expressed that he was greater than 90 percent improved.
CME AND NEW FACULTY

Upcoming Webinar CME Opportunity

Two exciting days of learning and exchange of ideas are in store for participants in an interactive, international CME Web-symposium entitled “Tricks of the Trade in Urology: Innovative Solutions to Common Problems.” The event will be held on Nov. 18-19, 2010, and will provide a forum for urologists to present their new ideas in all aspects of urological conditions to other surgeons around the world. You can participate from the comfort of your office or home, using any computer with Internet access. Sections will include:

- Female Urology
- Pediatric Urology
- Endourology
- Oncology
- Laparoscopy
- Ablative Therapies
- Robotics
- Laparoendoscopic Single Site Surgery / Natural Orifice Transluminal Endoscopic Surgery (LESS / NOTES)

The event also will feature videos from distinguished physicians highlighting innovative techniques, interesting cases or new therapies. For Webinar program details and to register, go to http://casemed.case.edu/cme/activities/calendar.cfm.

New Faculty

The University Hospitals Urology Institute welcomed two new faculty members this past summer.

Lynn L. Woo, MD

Lynn L. Woo

Robert Abouassaly, MD

Robert Abouassaly

Lynn L. Woo, MD, has joined the Center for Pediatric Urology. Dr. Woo recently completed a fellowship in Pediatric Urology at Vanderbilt Medical Center in Nashville, where her work included researching mesenchymal stem cell recruitment and function in the setting of bladder outlet obstruction and bladder fibrosis. She earned her medical degree from the University of Iowa College of Medicine.

Robert Abouassaly, MD, has joined the Center for Urologic Oncology. Dr. Abouassaly studied medicine at McGill University in Montreal, completed his urology residency at the Cleveland Clinic and recently finished a fellowship in Urologic Oncology at the University of Toronto, where he also earned a Master’s degree in Clinical Epidemiology. His research interests include health services and outcomes research in urologic malignancy (including prostate, kidney, bladder and testicular cancers).

Exchange Program Selection

Hui Zhu, MD, Urologist, University Hospitals Urology Institute, Associate Professor, Case Western Reserve University School of Medicine, was selected as one of the four 2010 American Urological Association/Chinese Urological Association (CUA) Academic Exchange Program scholars. The program is designed to help young academic urologists benefit from sharing their knowledge and experiences and to facilitate collaborative medical advances. Dr. Zhu will spend a month at urology institutes in China and will attend the CUA annual meeting in Xi’an, China.

Your Feedback is Important

As a medical professional, your input is invaluable in helping us shape future issues of UH Innovations In Urology. We want to know what's important to you. Do you want to read about cutting-edge research, learn about the latest technology, or hear firsthand case studies of how others in your specialty are improving and saving lives? Tell us what you want to read about and your name will be entered to win one of two Apple iPads! Simply visit UHhospitals.org/innovations.