

## INSIDE THIS ISSUE

### FEATURE ARTICLES

- Surgical Management of LUTS Attributed to BPH
- Active Surveillance for Early Stage Prostate Cancer
- Stone Removal and UTIs
- Brachytherapy Monotherapy
- Emphysematous Spermatic Cord Abscess
- Botulinum Neurotoxin for Sexual Dysfunction
- Small Renal Mass
- Dietary Induced Hyperoxaluria

### FEATURE COLUMNS

- Winter Board of Directors Actions and Updates
- 24/7 Educational Activities
- Artificial Intelligence in Urological Research
- Women's Health Resources and Initiatives

### HAVE YOU READ?

### PRACTICE TIPS & TRICKS

## FROM THE *AUA President*

# Standing Together as a Specialty: Uniting to Affect Change



**John H. Lynch, MD, FACS**  
Washington, D.C.

As my term as President of the American Urological Association (AUA)

comes to an end, I cannot help but reflect on several thoughts I initially shared in my inaugural address: "It is imperative the AUA continues to grow and change, and to provide the knowledge necessary...for a career of lifelong learning." During the last year I have been proud to lead an organization that works tirelessly to ensure its members are provided

with the tools, resources and support necessary to meet the wide-ranging and ever growing demands of our specialty.

As it stands, the AUA remains the premier urological association with nearly 22,000 members throughout the world who share a common mission. In the last 12 months we welcomed more than 2,200 new members to the AUA, representing the largest growth the association has experienced in a single year. With international, resident/fellow and medical/graduate student membership categories accounting for more than half of member growth in 2019,

it is clear now more than ever that the organization continues to widen its impact globally as well as provide a solid foundation for the future. This is a testament to the continued efforts of AUA Secretary Dr. John Denstedt, our 3 AUA Assistant Secretaries, our international partners and our members.

It was also especially exciting to welcome hundreds of future urologists via the 2020 Urology Residency Match. An annual rite of passage for medical students, this year's match not only had the most applicants since 2014, but also saw a record-setting 86% of female participants match with programs, which is a welcomed sign of increasing diversity in urology.

Discovery is at the heart of what we do, and the scientific research undertaken within urology has the capacity to improve human lives in ways

virtually unimaginable a generation ago. This past year our Foundation, the Urology Care Foundation, provided nearly \$1.5 million in research funding to more than 70 researchers whose efforts will keep us at the forefront for developing innovative ideas and treatments aimed at improving the lives of our patients. We must continue to support our young scientists, as we recognize the cures of tomorrow exist in the labs of today.

Led by the efforts of Dr. Aria Olumi, AUA's research initiatives also continued to expand with the introduction of our new research focused IMPACT magazine, the launch of a new research specific educational course on *AUAUniversity*, a cohosted StoneLab Scientific Symposium with the Endourological Society, and

▼ Continued on page 2

# 2020 Advanced Prostate Cancer Guideline



**Michael S. Cookson, MD, MMHC, FACS**  
Vice Chair, AUA  
Advanced Prostate  
Cancer Guidelines 2020  
Norman, Oklahoma



**William Lowrance, MD, MPH, MBA**  
Chair, AUA Advanced  
Prostate Cancer  
Guidelines 2020  
Salt Lake City, Utah

remains the second leading cause of cancer deaths in this population. Approximately 175,000 new diagnoses of prostate cancer and more than 31,000 deaths were estimated in the U.S. in 2019.<sup>1</sup> As the management of advanced prostate cancer continues to rapidly evolve, clinicians are challenged to remain up to date and informed with respect to the multitude of diagnostic and treatment options available for the care of these patients.

The increasing complexity of advanced prostate cancer management underscores the need for the

▼ Continued on page 3

Prostate cancer is the most commonly diagnosed solid organ malignancy in men in the United States and

NON-PROFIT ORG.  
U.S. POSTAGE  
PAID  
PERMIT NO. 797  
RICHMOND, VA

American Urological Association  
1000 Corporate Boulevard  
Linthicum, Maryland 21090

## From the AUA President

▼ Continued from page 1

the second annual Bladder Cancer Research Symposium with the Johns Hopkins University Greenberg Bladder Cancer Institute.

As a leading advocate for the specialty of urology, the AUA is always working to communicate members' concerns to leaders at the legislative and regulatory levels. Under the leadership of Dr. Christopher Gonzalez, the AUA was able to successfully move its advocacy agenda forward on such key issues as physician reimbursement, preserving men's access to prostate cancer screening and physician workforce shortages, to name a few. Collaborating with more than 50 patient and research advocacy organizations, AUA's Washington, D.C. team worked to elevate awareness about urological conditions, improve access to screenings and health care treatments, and promote increased funding for urological research. Furthermore, AUAPAC, AUA's political action committee, transitioned from its first year and continues to serve as a means to provide urologists throughout the country a strong voice in our nation's capital.

Dr. Victor Nitti has overseen the future of education for urologists and urological health care professionals worldwide by identifying next generation content, learning platforms and learning modalities, ensuring our members continue to receive quality, evidence-based education for years to come. As a compliment to its domestic reach, the AUA has developed a strong global community through its international membership and partners, and further increased the exchange of knowledge, education and networking opportunities among urologists worldwide. Whether through exchange programs, lectures and courses being offered in many countries around the world, the AUA continues its mission to advance urological patient care through global education.

None of these incredible accomplishments would have been possible without the more than 500 AUA members who volunteer their time, talent and expertise on AUA and Urology Care Foundation boards, councils, committees, work groups and guideline panels, and I am incredibly grateful to all of you.

I am also proud of the recently

announced "The Urology Care Foundation Humanitarian Award" and "The Urology Care Foundation Humanitarian Grant Program," new international initiatives recently announced by Urology Care Foundation President Dr. Harris Nagler. The Humanitarian Award recognizes an individual or organization for demonstrated commitment to improving access to quality urological health care in underserved populations. The Humanitarian Grant Program provides grants to support individuals and organizations who provide direct urological care to individuals and communities in underserved areas within or outside the United States. These programs truly exemplify the many patient missions being carried out globally.

In the spirit of true humanitarianism, I am proud to share that the AUA contributed \$150,000 to the Foundation to help establish their first endowment and contributed significant additional funds for the Foundation to match other grants and establish future endowments. I encourage you to donate to the Humanitarian Grant Program to help support those who give of themselves without remuneration and respond to the many men, women and children in need.

In my 2019 inaugural address I also stated: "As we look to the future, we must be united as a specialty. United, we have the opportunity to affect change." Never could I have imagined that less than 1 year after I wrote those words the world would be facing a global pandemic the likes of which none of us has seen in our lifetime. Those few words from my address last year resonate with me now more than ever.

The COVID-19 crisis has altered our lives professionally and personally in unthinkable ways. Families are being sheltered, employees are working from home, and urologists and urological health care professionals around the world are being called to serve their communities well outside of their traditional area of expertise. As we rise to this incredible challenge, I am amazed but not surprised by the countless stories I've heard of our members in every corner of the world stepping up to help however possible and provide care in areas (from a Level I trauma center to a solo practice and everything between) they do not customarily support. These

unprecedented circumstances also led the AUA to make the difficult but necessary decisions to postpone the Annual Urology Advocacy Summit and cancel the AUA Annual Meeting, both of which were scheduled to take place in Washington, D.C.

The Annual Urology Advocacy Summit will now take place August 31–September 2, and attendees can look forward to working together to strengthen and unify the voice of urology on policy matters impacting our practices and patients.

Unfortunately, given the logistics that go into organizing a meeting the size of AUA's annual meeting, we are unable to reschedule AUA2020. This cancellation becomes just the fifth time in the organization's history an annual meeting will not be held (prior instances were 2 years during World War I and 2 years during World War II). While deeply disappointed many colleagues and friends will not be coming together in Washington D.C. this month, I am so very proud to be part of an organization that has leveraged the technology at our disposal to begin sharing much of the science, abstracts, surgical videos, clinical education and more, underscoring our specialty's innovative and unwavering spirit.

Never in my medical career have I seen anything close to what the world is experiencing today but I am proud to stand alongside each of you as we navigate this difficult and challenging time together. As our members know, the AUA works to promote the highest standards of urological clinical care via the 3 primary pillars of education, research and the formulation of health care policy. However, advancing urology is more than that as it also means furthering the specialty in ways we might not traditionally think of, like the time, effort and sacrifices being made for the greater good of urology and the medical community as a whole.

It has always been a pleasure to be a member of the AUA but it has been my very distinct honor to serve as President of an organization with such a steadfast commitment to the medical community and patients worldwide. The future of our specialty is incredibly bright, and I will be forever grateful to be a small part of its history. ♦

# AUA NEWS

May 2020

Volume 25 | Issue 5

### EDITOR IN CHIEF

John D. Denstedt, MD, FRCSC, FACS, FCAHS  
London, Ontario, Canada

### Associate Editors

Sam S. Chang, MD  
Nashville, Tennessee  
Amy E. Krambeck, MD  
Indianapolis, Indiana  
Jeremy B. Myers, MD  
Salt Lake City, Utah  
David F. Penson, MD, MPH  
Nashville, Tennessee  
David Rapp, MD  
Charlottesville, Virginia  
Hossein Sadeghi-Nejad, MD, CM  
Hackensack, New Jersey  
Aseem Shukla, MD  
Philadelphia, Pennsylvania

### Spanish Edition Editor

Alejandro Remigio Rodriguez, MD  
Rochester, New York

### Executive Editor

Patricia Banks, Executive Vice President  
Marketing, Communications, Publications & Member Engagement  
American Urological Association  
1000 Corporate Boulevard  
Linthicum, Maryland 21090

### Managing Editor

Dorsey Mills  
Publications Department  
American Urological Association  
1000 Corporate Boulevard  
Linthicum, Maryland 21090

### Production

Cenveo Publisher Services  
2901 Byrdhill Road  
Richmond, VA 23228

### National Sales Manager

The Walchli Tauber Group  
2225 Old Emmorton Road, Suite 201  
Bel Air, MD 21015  
Phone: 443-512-8899 ext. 101

### American Urological Association

#### 2019–2020 AUA Officers

#### President

John H. Lynch, MD, FACS

#### President-elect

Scott K. Swanson, MD, FACS

#### Immediate Past President

Robert C. Flanigan, MD, FACS

Secretary John D. Denstedt, MD, FRCSC,  
FACS, FCAHS

Treasurer David F. Green, MD, FACS

**AUA News** is the official newsmagazine of the American Urological Association, located at 1000 Corporate Blvd., Linthicum, MD 21090, and is a function of the AUA Education and Research, Inc. **AUA News** is published 12 times a year by the American Urological Association. Copyright © 2020 by American Urological Association Education and Research, Inc.. No part of this publication may be reproduced in any form or language without written permission from the publisher. Published free of charge for AUA membership. Annual non-member subscription rates: individual \$110 (\$155 foreign); institution \$135 (\$180 foreign); industry \$65 (\$135 foreign). U.S. POSTMASTER: Send address changes to **AUA News**, American Urological Association, 1000 Corporate Blvd., Linthicum, MD 21090. Library of Congress ISSN: 1088-7350. All correspondence on editorial matters should be addressed to: Executive Editor, American Urological Association, 1000 Corporate Boulevard, Linthicum, MD 21090.

**Disclaimer:** The statements and opinions contained in the articles in **AUA News** are solely those of the individual authors and contributors and not of the American Urological Association. The appearance of advertisements in **AUA News** is not a warranty, endorsement or approval of the products or services advertised or of their effectiveness, quality or safety. The content of this publication may contain discussion of off-label uses of some of the agents mentioned. Please consult the prescribing information for full disclosures of approved uses. The American Urological Association disclaims responsibility for any injury to persons or property resulting from any ideas or products referred to in the articles or advertisements.

## Advanced Prostate Cancer Guideline

▼ Continued from page 1

development of the current clinical practice guideline to provide a rational basis for the treatment of patients with advanced disease based on available published data. The 2020 AUA advanced prostate cancer guideline is an expansion of the castration resistant prostate cancer (CRPC) guideline originally published in 2013 and is intended to address a number of advanced disease states, including nonmetastatic biochemically recurrent prostate cancer, metastatic hormone sensitive prostate cancer, and nonmetastatic and metastatic CRPC.

The advanced prostate cancer guideline explores the currently available prognostic and treatment modalities available for each disease state while acknowledging ongoing research in the field and current unmet needs. Treatments evaluated in the guideline include conventional androgen deprivation therapy alone and in combination with first and second line antiandrogens, chemotherapy, radiation therapy, surgery,

radiopharmaceuticals, immunotherapy and surveillance strategies.

The guideline further explores appropriate use of conventional and advanced imaging as well as genetic (including germline and somatic) testing. Outcomes of interest are overall survival, prostate cancer mortality, progression free survival, prostate specific antigen, progression-free survival, failure-free survival, metastases-free survival, time to metastases, time to progression, skeletal events and adverse events.

Central to this guideline is the understanding that multimodality approaches and integration of care are critical to improving the treatment of men with advanced prostate cancer. Multidisciplinary clinics and the resulting multimodality treatment approaches can optimize treatment selection, maximize results, and minimize overtreatment and side effects.

As the therapeutic landscape progresses to include further combinations of systemic therapies with or without local therapies, advances in imaging, and germline and somatic genetic testing, treatment of advanced prostate cancer increasingly

must embrace such management approaches. Team members should include urologists, medical oncologists and radiation oncologists at a minimum when supporting treatment decisions for advanced disease are made. While focusing on disease treatment, patient care must also address issues related to quality of life and symptom management. As such, additional specialists may also include genitourinary pathology, genetic counseling, palliative care and holistic specialists in addition to primary care.

Although dramatic recent advances have been made, many unmet needs remain in prostate cancer management. Personalized care with predictive markers for treatment selection based on tumor and host biology have not yet been achieved. There has been movement toward identification of prognostic markers and molecular markers based on immunohistochemistry and genomic signatures but these have yet to yield predictive results.

As we move forward in the field, we need to focus on the biological make-up of tumors and how this can be

better leveraged to identify treatment options for patients. Furthermore, advanced imaging technologies using novel tracers have emerged as sensitive and specific tools to detect metastatic disease at an earlier stage in the progression timeline. However, uncertainty remains as to how future image directed therapies might impact oncologic outcomes.

Historically, the median survival for men with metastatic CRPC was less than 2 years<sup>2</sup> but due to several factors, including standardized definitions, the impact of new therapies and the sequencing of therapies, the median survival has now more than doubled. It is against this backdrop that the panel provides evidence-based guidance for the management of advanced prostate cancer and looks to the future with cautious optimism.



1. Siegel RL, Miller KD and Jemal A : Cancer statistics, 2019. *CA Cancer J Clin* 2019; **69**: 7.
2. Moreira DM, Howard LE, Sourbeer KN et al: Predicting time from metastasis to overall survival in castration-resistant prostate cancer: results from SEARCH. *Clin Genitourin Cancer* 2017; **15**: 60.

## Surgical Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia: AUA Guideline Update



Steven A. Kaplan, MD  
New York, New York

Male lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH)

are common in men and can have negative effects on quality of life (QOL). It is the hope that this AUA guideline becomes a reference for effective evidence-based surgical management of LUTS/BPH.

The evidence review team searched Ovid MEDLINE®, the Cochrane Library and the Agency for Healthcare Research and Quality databases to identify randomized controlled trials, clinical controlled trials, systematic reviews/meta-analyses and observational studies published and indexed between January 2007 and September 2017. Note that additional studies published outside of this date

range may be included to inform background sections or provide historical context.

Systematic reviews and meta-analyses were searched to identify additional eligible studies. The review team also reviewed articles for inclusion identified by the panel. Search terms included Medical Subject Headings (MeSH) and keywords for procedures, devices and conditions related to LUTS or BPH. Limits were used to restrict the search to English language publications.

The AUA update literature review process, in which an additional systematic review is conducted periodically to maintain guideline currency with newly published relevant literature, was conducted in January 2019. This review identified an additional 9 articles relevant to treatment. These articles were added to the database, and AUA's qualitative and quantitative analyses were updated

as appropriate. The review panel determined that the update review warranted a targeted update to the document, thereby creating the May 2019 amendment.

Another updated review was conducted in September 2019. Two additional articles relevant to BPH treatment were identified from this update and, therefore, the current guideline reflects relevant literature published through September 2019.

When sufficient evidence existed the body of evidence was assigned a strength rating of A (high), B (moderate) or C (low) for support of strong, moderate or conditional recommendations. In the absence of sufficient evidence, additional information is provided as Clinical Principles and Expert Opinions.

The new iteration of guidelines will have statements regarding the diagnosis and evaluation of BPH as well as the treatment and re-treatment with minimally invasive and surgical therapies. The panel is also reviewing medical therapy for BPH but formal guidelines will not be presented until 2021.

More specifically, the guidelines will have statements on water vapor thermal therapy, prostatic urethral lift and prostate arterial embolization.<sup>1-3</sup>

In early 2019 aquablation was added to the guidelines as new literature emerged, and this will be updated as well.<sup>4</sup>

Gaps in knowledge remain. Therefore, opportunities for discovery ensue. These opportunities include but are not limited to many unanswered questions related to the role of inflammation, metabolic dysfunction, obesity and environmental factors in etiology as well as the role of behavior modification, self-management, definition of treatment failures and evolving therapeutic algorithms in the prevention and progression of disease. ◆

1. Rukstalis D, Grier D, Stroup SP et al: Prostatic urethral lift (PUL) for obstructive median lobes: 12 month results of the MedLift Study. *Prostate Cancer Prostatic Dis* 2019; **22**: 411.
2. McVary KT, Rogers T and Roehrborn CG: Rezūm water vapor thermal therapy from lower urinary tract symptoms associated with benign prostatic hyperplasia: 4-year results from randomized controlled study. *Urology* 2019; **126**: 171.
3. Abt D, Hechelhammer L, Müllhaupt G et al: Comparison of prostatic artery embolization (PAE) versus transurethral resection of the prostate (TURP) for benign prostatic hyperplasia: randomized, open label, non-inferiority trial. *BMJ* 2018; **361**: k2338.
4. Gilling P, Barber N, Bidair M et al: Randomized controlled trial of aquablation versus transurethral resection of the prostate in benign prostatic hyperplasia: one-year outcomes. *Urology* 2019; **125**: 169.

## Active Surveillance for Early Stage Prostate Cancer—The Past or the Future?



**Peter R. Carroll, MD, MPH**  
San Francisco, California

Two decades ago active surveillance (AS) for early stage prostate cancer rather than immediate treatment with surgery or radiation would have been unthinkable. Fast-forward to the present and active surveillance for those with very low and low risk disease has been endorsed by all major international guidelines.

The impetus for this sea change in approach was clear evidence of overdiagnosis (and resulting overtreatment) that came with aggressive prostate specific antigen (PSA) testing as well as better knowledge about the biology and natural history of early stage disease. The knowledge that came from 3 large North American cohorts and additional trials in Europe has demonstrated the clear safety of this approach. Although treatment rates at 5 and 10 years approach 30% and 50%, respectively, there is an exceedingly low rate of metastases at long-term followup.

Although AS prevalence has clearly increased in recent years, its use remains variable. There may be a variety of reasons for this variability including the uncertainty patients and physicians have that they may be missing clinically significant disease that was not sampled by standard evaluation. Newly refined and even standard technology has addressed this particular issue. Gene expression profiling of the biopsy specimens has been shown to better identify those who may be harboring higher grade and/or stage disease and those at risk of progression on AS. In addition, multiparametric (mp) magnetic resonance imaging (MRI) addresses the same concern (under sampling).

However, even old technology like the simple calculation of PSA density (PSAD) has considerable value. Those with a PSAD greater than 0.15 are at higher risk of disease progression. Concerning results using any of these markers does not mean that men need to be treated but should prompt early reassessment including early confirmatory testing (fusion guided biopsy).

The controversies surrounding AS currently center on whether young

men, African American men or those with higher grade disease (Gleason Grade 3 or 4) are candidates for such an approach. Younger men have either an equivalent or lower rate of disease progression and, therefore, remain candidates for AS. However, this population needs to be advised that the likelihood of future treatment remains high because of generally low comorbidity and a longer life expectancy. African American men represent a small percentage included in the major cohorts that have formed the basis of our knowledge on AS. However, assessment by gene expression profiling and mpMRI appears reliable in such men. Therefore, treatment recommendations should not be made on the basis of ethnicity alone.

The most controversial subject is whether men with Gleason Grade 3 or 4 disease should be offered AS. Clearly this population is at higher risk of disease progression. However, it appears that volume rather than grade alone identifies higher risk. Therefore, men with a low volume of secondary pattern 4 may be acceptable candidates for AS. Such patients are ideal candidates for advanced testing with mpMRI and gene expression profiling. It also appears that subtyping pattern 4 cells into histological subtypes (cribriform, glomerular, fused etc) identifies higher risk. Lastly, clinicians need to be

concerned about accurate grading in men with very low volume, secondary pattern 4 disease as tangential sectioning of tissue can misclassify low grade disease as being higher grade.

Although many believe the future of AS remains bright, a few changes in our diagnostic pathway and/or treatment paradigm may change this belief. It is clear that immediate biopsy in patients with elevated PSA leads to unnecessary biopsies (negative biopsies) or the detection of low grade disease that does not require treatment. Therefore, biopsy rates can be reduced by secondary screenings in men with elevated serum PSA (serum and urine markers as well as mpMRI), which will likely lead to fewer patients diagnosed with low risk disease. New and aggressive biopsy techniques are identifying patients who seem to be candidates for focal therapy, many of whom are perfect candidates for AS. Urologists should not routinely treat patients who are good candidates for AS with focal forms of treatment.

Finally, active surveillance as currently practiced with repeated biopsies needs to be less onerous and expensive. New information that predicts the risk of upgrading over time (PSAD, MRI, gene expression results, negative confirmatory biopsies etc) has emerged, allowing less intensive and more efficient surveillance of those at low risk. ♦

## Using the AUA/SUFU Recurrent UTI Guidelines to Better Meet Patient Needs



**Una J. Lee, MD**  
Seattle, Washington

When we see a woman with recurrent urinary tract infections (UTIs), our goal should be for that patient to leave highly satisfied with the clinic visit. She should have her important questions answered, have her level of distress alleviated, gain a deeper understanding of the problem and have a mutually agreed upon evaluation, treatment and prevention plan that gives her structure and hope. As physicians we have the necessary medical knowledge but it is equally if not more, important to leverage our interpersonal skills in this service

oriented profession.

Recurrent UTIs are frustrating to patients as well as primary care physicians and urologists for various reasons. There is often a gap between what patients want and what physicians provide.<sup>1</sup> It is a learned skill to successfully assess and counsel patients with recurrent UTIs as they arrive with a wide spectrum of concerns, knowledge, expectations and desires. As urologists we have all seen and evaluated patients with recurrent UTIs, and I would challenge us all to think about what we can improve to better meet patient needs and implement small changes that are patient centered.

This way of framing the visit is based on several sources, the first of which is “The Four Habits Model of

Physician Communication.”<sup>2</sup> The second is qualitative research on women’s experiences with recurrent UTIs,<sup>3</sup> and the third is the AUA/CUA (Canadian Urological Association)/SUFU (Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction) guidelines on recurrent uncomplicated urinary tract infections in women.<sup>4</sup>

The Four Habits is a well-accepted and widely used model that has been associated with an increase in patient satisfaction. The half-day to full-day course teaches us to break out of the doctor centered medical interview and models key behaviors that prioritize patient needs. The Four Habits are 1) invest in the beginning of the visit and build rapport, 2) elicit the patient’s perspective, 3) demonstrate empathy and 4) involve the patient at the end of the visit in designing a treatment plan (fig. 1).

An important way of investing in the beginning of the visit is to ask patients upfront, “What are your

concerns?” and then make sure to answer their question(s) in language they understand. Qualitative research on women with recurrent UTIs has shown that they are fearful of recurrent UTIs as a harbinger of a larger underlying disease.<sup>5</sup> If they express that they are worried that they have cancer or that something else is wrong, then be sure to circle back and explain why something serious is not the cause of the UTIs but that they have an increased vulnerability to UTIs that can be alleviated through targeted strategies.

Eliciting patient perspective is a critical step in developing rapport with patients and understanding their goals. By summarizing themes and using illustrative quotes, qualitative research allows providers to walk in women’s shoes and see the world from their viewpoints.<sup>6,7</sup> Women with recurrent UTIs describe symptoms that are beyond the textbooks, such

**Recurrent UTI Guidelines**

▼ Continued from page 4

as “a terrible scorch,” “peeing barb wire” and “a vile infection that causes shaking and shivering, terrible diarrhea and waves of nausea.” Relief has been described as “happiness” in the bladder.<sup>8</sup>

Patients report that UTIs detrimentally impact every aspect of their lives (sexual relationships, work productivity, home responsibilities and social lives including anxiety

about future plans), thus leading to a heightened level of distress as well as increased association of depression and anxiety.<sup>9-11</sup> Women who articulate being thankful for antibiotics are also fearful of their risks, resistances and side effects. They express interest in complementary and alternative therapies including dietary and lifestyle changes as these options give them a greater sense of control and empowerment, allowing them to heal instead of suppressing the disease process.<sup>8</sup>

Women also perceive doctors as villains or heroes based on their interactions. They feel dismissed and judged by some providers and acknowledged and validated by conscientious, caring and supportive physicians. The words we say and the way we communicate are powerfully felt by patients who are desperate for a cure and a cause. Saying, “I don’t know why you are getting these UTIs,” “It’s normal to get UTIs” or “Try to stay clean down there” can come across as dismissive, judgmental and uncaring.

Instead, physicians can express empathy and validate concerns<sup>1</sup> with phrases like, “It sounds like these urinary infections have been upsetting and stressful.” Doctors can also frame diagnoses and provide education by saying, “These UTIs are occurring frequently because there is a low level of estrogen in that area of the body which is making you more vulnerable to UTIs.” Patient education on judicious antibiotics use is also key,

▼ Continued on page 6

## THE FOUR HABITS MODEL

Habit	Skills	Techniques and Examples	Payoff
<b>Invest in the Beginning</b>	Create rapport quickly	<ul style="list-style-type: none"> <li>• Introduce yourself to everyone in the room</li> <li>• Acknowledge wait</li> <li>• Convey knowledge of patient’s history by commenting on prior visit or problem</li> <li>• Attend to the patient’s comfort</li> <li>• Make a social comment or ask a non-medical question to put patient at ease</li> <li>• Adapt your language, pace, and posture in response to the patient</li> </ul>	<ul style="list-style-type: none"> <li>• Establishes a welcoming atmosphere</li> <li>• Allows faster access to real reason for visit</li> <li>• Increases diagnostic accuracy</li> <li>• Requires less work</li> <li>• Prevents “Oh by the way...” at the end of the visit</li> <li>• Facilitates negotiating an agenda</li> <li>• Decreases potential for conflict</li> </ul>
	Draw out the patient’s concerns	<ul style="list-style-type: none"> <li>• Start with open-ended questions:                             <ul style="list-style-type: none"> <li>- “What would you like help with today?” Or, “I understand that you’re here for ... Could you tell me more about that?”</li> <li>- “What else?”</li> </ul> </li> <li>• Speak directly with the patient when using an interpreter</li> </ul>	
	Plan the visit with the patient	<ul style="list-style-type: none"> <li>• Repeat concerns back to check understanding</li> <li>• Let the patient know what to expect: “How about if we start with talking more about..., then I’ll do an exam, and then we’ll go over possible tests/ways to treat this? Sound OK?”</li> <li>• Prioritize when necessary: “Let’s make sure we talk about X and Y. It sounds like you also want to make sure we cover Z. If we can’t get to the other concerns, let’s...”</li> </ul>	
<b>Elicit the Patient’s Perspective</b>	Ask for the patient’s ideas	<ul style="list-style-type: none"> <li>• Assess the patient’s point of view:                             <ul style="list-style-type: none"> <li>- “What do you think is causing your symptoms?”</li> <li>- “What worries you most about this problem?”</li> </ul> </li> <li>• Ask about ideas from significant others</li> </ul>	<ul style="list-style-type: none"> <li>• Respects diversity</li> <li>• Allows the patient to provide important diagnostic clues</li> <li>• Surfaces hidden concerns</li> <li>• Reveals use of alternative treatments or requests for tests</li> <li>• Improves diagnosis of depression and anxiety</li> </ul>
	Elicit specific requests	<ul style="list-style-type: none"> <li>• Determine the patient’s goal in seeking care: “when you’ve been thinking about this visit, how were you hoping I could help?”</li> </ul>	
	Explore the impact on the patient’s life	<ul style="list-style-type: none"> <li>• Check context: “How has the illness affected your daily activities/work/family?”</li> </ul>	
<b>Demonstrate Empathy</b>	Be open to the patient’s emotions	<ul style="list-style-type: none"> <li>• Assess changes in body language and voice tone</li> <li>• Look for opportunities to use brief empathic comments or gestures</li> </ul>	<ul style="list-style-type: none"> <li>• Adds depth and meaning to the visit</li> <li>• Builds trust, leading to better diagnostic information, adherence, and outcomes</li> <li>• Makes limit-setting or saying “no” easier</li> </ul>
	Make at least one empathic statement	<ul style="list-style-type: none"> <li>• Name a likely emotion: “That sounds really upsetting.”</li> <li>• Compliment the patient on efforts to address own problem</li> </ul>	
	Convey empathy nonverbally	<ul style="list-style-type: none"> <li>• Use a pause, touch, or a facial expression</li> </ul>	
	Be aware of your own reactions	<ul style="list-style-type: none"> <li>• Use your emotional response as a clue to what the patient might be feeling</li> <li>• Take a brief time-out if necessary</li> </ul>	
<b>Invest in the End</b>	Deliver diagnostic information	<ul style="list-style-type: none"> <li>• Frame diagnosis in terms of patient’s original concerns</li> <li>• Test for patient comprehension</li> </ul>	<ul style="list-style-type: none"> <li>• Increases potential for collaboration</li> <li>• Impacts health outcomes</li> <li>• Improves adherence</li> <li>• Reduces return calls and visits</li> <li>• Encourages self care</li> </ul>
	Provide education	<ul style="list-style-type: none"> <li>• Explain rationale for tests and treatments</li> <li>• Review possible side effects and expected course of recovery</li> <li>• Recommend lifestyle changes</li> <li>• Provide written materials and refer to other resources (Healthwise Handbook)</li> </ul>	
	Involve the patient in making decisions	<ul style="list-style-type: none"> <li>• Discuss treatment goals</li> <li>• Explore options, listening for the patient’s preferences</li> <li>• Set limits respectfully: “I can understand how getting that test makes sense to you. From my point of view, since the results won’t help us diagnose or treat your symptoms, I suggest we consider this instead.”</li> <li>• Assess the patient’s ability and motivation to carry out plan</li> </ul>	
	Complete the visit	<ul style="list-style-type: none"> <li>• Ask for additional questions: “Anything else you wanted to talk about?”</li> <li>• Assess satisfaction: “Did you get what you needed?”</li> <li>• Reassure the patient of ongoing care</li> </ul>	

Figure 1. New approach to medical interview: the Four Habits Model. Reprinted with permission.<sup>2</sup>

## Recurrent UTI Guidelines

▼ Continued from page 5

and patients are receptive when the reasoning is explained in terms they can understand.

I would encourage all urologists to read the entire content of the AUA guidelines on recurrent UTIs<sup>4</sup> as there is a wealth of information in the document that can be delivered in a patient friendly way to educate patients on the evidence-based recommendations. The 1-page diagnosis and treatment algorithm from the guideline can be printed as a handout and used as a visual tool to facilitate a discussion on the various therapeutic options resulting in a mutually agreed upon plan (fig. 2).

Step 4 of the Four Habits includes delivering the diagnosis, providing education, and involving the patient in the evaluation and treatment plan. One gap between patients and doctors is that patients are focused on improving care for acute UTIs while physicians are focused on prophylaxis and efficacious management of the recurrent UTIs as a chronic condition.<sup>5</sup> To address this discrepancy, physicians also need to create a plan for when acute UTI symptoms develop. This step is when physicians can educate patients on the importance of submitting specimens for urinalysis and culture as well as set expectations for next steps. Through patient education, shared decision making and managing expectations, the goal of patient satisfaction and high quality care of recurrent UTIs can be achieved.

Recurrent UTIs in women are a prevalent, costly and impactful problem that often cause a high level of patient distress. As physicians, we can elevate the quality of care that we provide to women through individualized patient centered communication that is grounded in sound evidence including antibiotic stewardship. ♦

1. Moskowitz D and Lee U: Patient distress in women with recurrent urinary tract infections: how can physicians better meet patients needs? *Curr Urol Rep* 2018; **19**: 97.
2. Frankel RM and Stein T: Getting the most out of the clinical encounter: the Four Habits Model. *Permanente J* 1999; **3**: 79.
3. Flower A, Bishop FL and Lewith G: How women manage recurrent urinary tract infections: an analysis of postings on a popular web forum. *BMC Fam Pract* 2014; **15**: 162.
4. Anger J, Lee U, Ackerman L et al: Recurrent Uncomplicated Urinary Tract Infections in Women: AUA/CUA/SUFU Guideline. American Urological Association 2019. Available at <https://www.auanet.org/guidelines/>

## Recurrent Uncomplicated Urinary Tract Infections in Women: AUA/CUA/SUFU Diagnosis & Treatment Algorithm

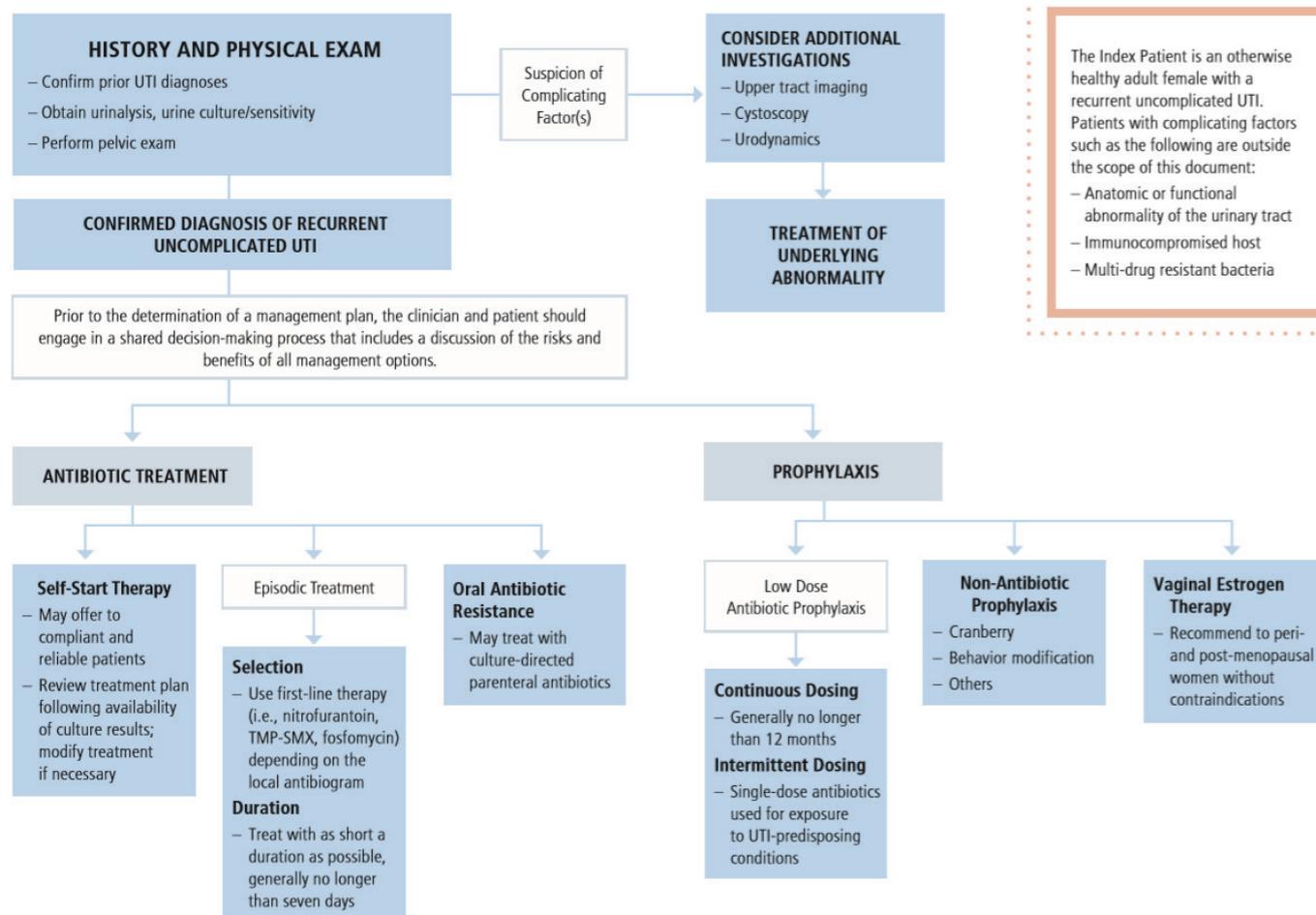


Figure 2. Recurrent uncomplicated UTIs in women: AUA/CUA/SUFU diagnosis & treatment algorithm.

### [recurrent-uti.](#)

5. Sadun T, Scott V, Thum L et al: Discrepancies in patient and physician perspectives on quality of care delivered to patients with recurrent urinary tract infections (abstract PD58-12). *J Urol*, suppl., 2019; **201**: e1033.
6. Eriksson I, Olofsson B, Gustafson Y et al: Older women's experiences of suffering from urinary tract infections. *J Clin Nurs* 2014; **23**: 1385.
7. Leydon GM, Turner S, Smith H et al: Women's views about management and cause of urinary tract infection: qualitative interview study. *BMJ* 2010; **340**: e279.
8. Alraek T and Baerheim A: 'An empty and happy feeling in the bladder...': health changes experienced by women after acupuncture for recurrent cystitis. *Complement Ther Med* 2001; **9**: 219.
9. Ellis AK and Verma S: Quality of life in women with urinary tract infections: is benign disease a misnomer? *J Am Board Fam Pract* 2000; **13**: 392.
10. Renard J, Ballarini S, Mascarenhas T et al: Recurrent lower urinary tract infections have a detrimental effect on patient quality of life: a prospective, observational study. *Infect Dis Ther* 2015; **4**: 125.
11. Wagenlehner F, Wullt B, Ballarini S et al: Social and economic burden of recurrent urinary tract infections and quality of life: a patient web-based study (GESPRIT). *Expert Rev Pharmacoecon Outcomes Res* 2018; **18**: 107.

## 2020 Practice Managers' Network

GIVE YOUR PRACTICE THE TOOLS THEY NEED TO OPTIMIZE YOUR BUSINESS OPERATIONS!

THE BEST  
\$349  
YOU'LL INVEST  
THIS YEAR!!

American Urological Association  
Advancing Urology

SUBSCRIBE TODAY!  
AUANET.ORG/PMN

# Complete Stone Removal May Eliminate Recurrent Urinary Tract Infections



Marcelino Rivera, MD



Deepak Agarwal, MD

Indianapolis, Indiana

Recurrent urinary tract infections (rUTIs), defined as 2 urinary tract infections (UTIs) in a 6-month period or more than 3 in 12 months, is a prevalent, costly disease afflicting women disproportionately more than men with evaluation and treatment costs approaching \$2 billion annually in the United States alone.<sup>1</sup> After a comprehensive history and physical examination confirming prior positive cultures when symptomatic, and a current urinalysis and culture are

performed, further contributing anatomic factors may be identified.

Per the AUA/CUA (Canadian Urological Association)/SUFU (Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction) guideline, while routine upper tract imaging for uncomplicated rUTIs is not recommended, if there is suspicion of complicating factors, upper tract imaging may be considered.<sup>1</sup> A significant number of patients who are referred to a urologist with a diagnosis of rUTIs already have had upper tract imaging obtained and stones identified.

While individuals with rUTIs may have upper tract stones identified during an evaluation, the degree to which urinary stones contribute to UTIs is poorly understood. Urological dogma has trained us to understand that certain bacteria, particularly urease splitting organisms, are known to

create infectious/struvite stones. Less is known about noninfectious stone disease and the influence on rUTIs or if metabolic stones can even harbor bacteria. Prior investigations into positive stone cultures in nonstruvite stone disease have demonstrated a microbiome attached to metabolic stones.<sup>2</sup>

A microbiome of urinary stones is now emerging as a result of advances in the ability to extract bacterial DNA via 16S rRNA gene sequencing. Common urinary bacteria and uncommon colonizers of the urinary tract have been identified using these advanced sequencing techniques.<sup>2</sup> However, whether these identified organisms are pathogenic and contribute to rUTIs is unknown. A suggestion of the presence of a stone as the source of rUTIs may be a recurrent identical organism on culture.<sup>3</sup> In patients with rUTIs and upper tract stones is the stone acting as a safe haven for these pathogenic bacteria only to seed the lower tract once treatment with antibiotics has been completed?

Omar et al performed one of the largest investigations of rUTIs and

upper tract urinary stones.<sup>4</sup> The study identified 120 patients confirmed to be stone-free on routine followup x-ray of the kidneys, ureters and bladder, and ultrasound following treatment with percutaneous nephrolithotomy (PCNL), extracorporeal shock wave lithotripsy (ESWL) or ureteroscopic (URS) stone removal.<sup>4</sup> Of the patients nearly 70% were female and PCNL was the most common procedure performed, followed by ESWL and ureteroscopy. Stone analysis included nonstruvite and struvite stones. Patients were then grouped into those with persistent rUTIs vs cured rUTIs at 1 year after stone removal. Of the patients 48% were cured of rUTIs at 1 year and those most likely to clear infections were associated with Escherichia coli positive urine cultures. However, Enterococcus was associated with failed clearance of recurrent infection. The authors concluded that individuals with E. coli rUTIs should be offered stone clearance.

Given the positive results of Omar et al<sup>4</sup> and previous work

▼ Continued on page 8

## AUA VIRTUAL EXPERIENCE

Access The Latest Education from AUA Right from Your Computer!  
All Programs are Offered as a Free AUA Member Benefit

### VIRTUAL SCIENCE – A NEW, MULTI-MEDIA REINVENTION OF THE AUA2020 POSTER & PODIUM SESSIONS

Abstract presentations will be available on May 15. AUA members will have access to slides and recorded audio presentations of the studies, to further enhance the educational experience.

### AUA LIVE – A TWO-DAY VIRTUAL EDUCATION EXPERIENCE!

On June 27-28, 2020 the AUA will host two days of select live-streamed educational programming, including keynote lectures, sessions on new clinical guidelines, semi-live surgeries, late-breaking science, industry updates and more. More details to come!

### AUA SUMMER SCHOOL – LIVE INSTRUCTIONAL COURSE WEBINARS

From June to August, AUA will launch two live instructional Webinars per week, with topics spanning the urologic clinical spectrum.

### RESEARCH WEEKEND – RECORDED WEBCASTS

Later this summer, the AUA will Webcast its popular research programs: Urologic Oncology Research Symposium, Basic Sciences Symposium, Challenges for Urologic Research and Early-Career Investigators Showcase.

### SURGICAL VIDEOS

This spring the AUA will publish all of the accepted Surgical Videos. Two new videos will be made available each week.

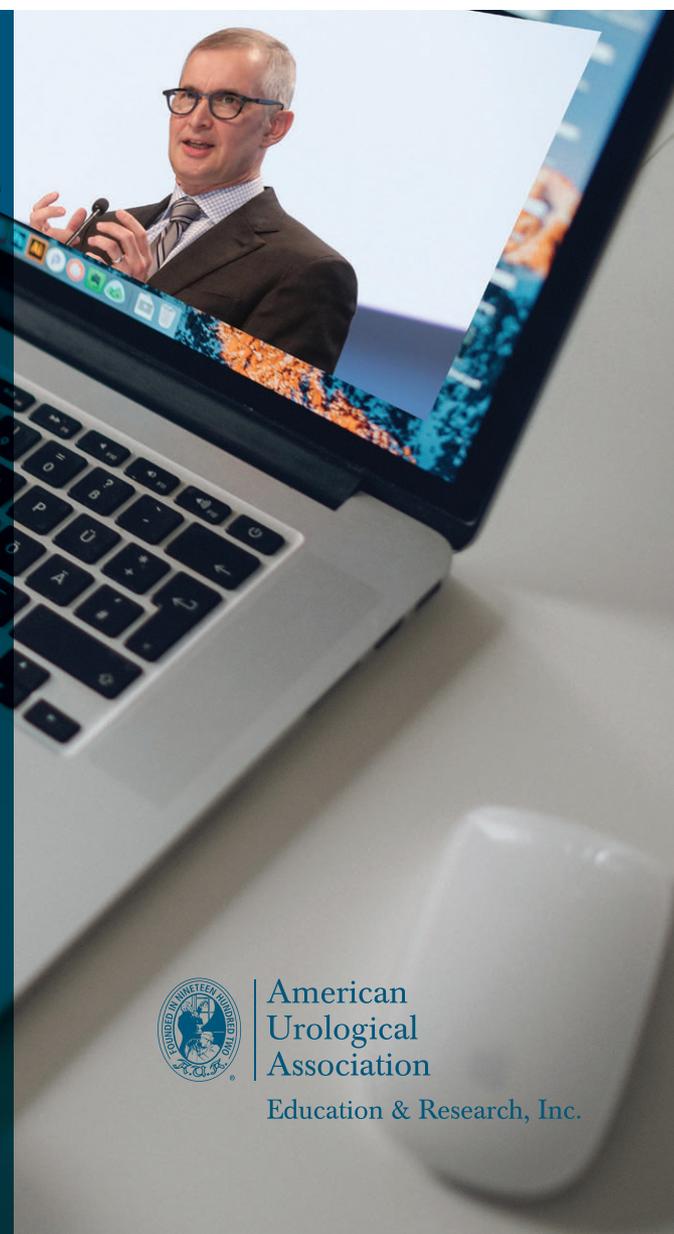
### PRACTICE MANAGEMENT PROGRAM – VIRTUAL LIVE MEETING

On May 15-16, the AUA will bring you six sessions on the topics impacting your urology practice.

### UROLOGIC CARE FOR THE ADVANCED PRACTICE PROVIDER – VIRTUAL LIVE MEETING

On May 16-17, the AUA will feature two full days of programming devoted to enhancing the education of APPs and other allied healthcare professionals.

Visit [AUA2020.org/VirtualExperience](https://AUA2020.org/VirtualExperience) for More Details!



American  
Urological  
Association

Education & Research, Inc.

## Stone Removal and UTIs

▼ Continued from page 7

demonstrating relatively high efficacy in eliminating rUTIs with stone removal, we evaluated an institutional cohort focused on a defined group of patients with rUTIs in the absence of an obstructing or symptomatic stone, or presence of struvite stone disease.<sup>5</sup> All patients underwent either URS or PCNL for stone removal due to higher stone-free rates and given the importance of rendering these particular patients as stone-free as possible. We identified 46 patients who met

criteria with a variety of organisms present in preoperative urine culture with *E. coli* and *Enterococcus* species as the most common. Stone culture results were positive in 54% and concordant with preoperative urine cultures in 67%. At a median followup of 2.9 years 89% of the cohort were free of rUTIs. Patients experienced an average of 3.1 UTIs in the year prior to intervention and only 0.5 UTIs annually thereafter. Only the presence of a residual stone fragment was significantly associated with rUTIs after intervention.

rUTI is a common and complex disease resulting in a high expenditure of health care dollars with a lack

of high quality evidence supporting clinical guidelines. We identified a subset of patients with nonobstructing, nonstruvite stone disease who appear to benefit clinically from stone removal. Residual stone fragments are a nidus for further UTIs in this patient population. Previous teaching that only struvite stone disease is associated with UTI appears to be limited, and individuals with rUTIs and upper tract stones appear to benefit greatly from complete stone clearance.

A better understanding of which patients with rUTIs would benefit most from stone removal is needed as well as further study toward a better understanding of the role of stone

microbiome of secondarily infected stones. ◆

1. Anger J, Lee U, Ackerman A et al: Recurrent uncomplicated urinary tract infections in women: AUA/CUA/SUFU guideline. *J Urol* 2019; **202**: 282.
2. Schwaderer AL and Wolfe AJ: The association between bacteria and urinary stones. *Ann Transl Med* 2017; **5**: 32.
3. Aslam S, Albo M and Brubaker L: Recurrent urinary tract infections in adult women. *JAMA* 2020; doi:10.1001/jama.2019.21377.
4. Omar M, Abdulwahab-Ahmed A, Chaparala H et al: Does stone removal help patients with recurrent urinary tract infections? *J Urol* 2015; **194**: 997.
5. Agarwal DK, Krambeck A, Sharma V et al: Treatment of non-obstructive, non-struvite urolithiasis is effective in treatment of recurrent urinary tract infections. *World J Urol* 2019; doi:10.1007/s00345-019-02977-3.

## Brachytherapy Monotherapy—a Treatment of the Past?



David D. Yang, MD



Marco Paciotti, MD



Martin T. King, MD,  
PhD



Quoc-Dien Trinh, MD

Boston, Massachusetts

Prostate brachytherapy is the implantation of radioactive sources directly into the prostate in order to deliver a high dose of radiation to the gland while minimizing radiation to normal tissues. The radioactive sources can be left in the prostate either permanently at a low dose rate (LDR) or temporarily at a high dose rate (HDR).

Brachytherapy monotherapy, along with external beam radiation therapy (EBRT) and radical prostatectomy, is recommended as one of the options for the definitive management of low risk and favorable intermediate risk prostate cancer based on guidelines from various professional organizations.<sup>1,2</sup> However, despite the endorsement of brachytherapy monotherapy for the management of favorable risk prostate cancer by professional societies, brachytherapy use for favorable risk disease has significantly decreased in recent years, particularly among patients who choose active treatment.<sup>3</sup>

A study of the National Cancer Database revealed that while approximately 30% of patients at low risk who received definitive local therapy were treated with brachytherapy in 2004, this rate had alarmingly decreased to

only about 15% during the course of 8 years. This decrease is likely caused by a variety of societal and economic factors. In particular, there is a mistaken perception that brachytherapy is an antiquated modality, despite high quality modern data outlined below which have consistently demonstrated brachytherapy to have excellent efficacy, a favorable side effect profile and cost effectiveness.

Brachytherapy monotherapy has reliably shown excellent long term cancer control outcomes, with 8- and 10-year biochemical control rates greater than 90% in properly selected patients with high quality implants.<sup>4-6</sup> Two small, prospective randomized trials did not demonstrate a difference in biochemical control between brachytherapy and radical prostatectomy for low risk disease.<sup>7,8</sup> These data are not novel, and no recent data have suggested that brachytherapy would be an inferior treatment in the appropriate settings.

In terms of morbidity and burden on the patient, brachytherapy offers several advantages compared to EBRT and radical prostatectomy. Compared to EBRT, which consists of daily radiation typically over the

course of 4 to 8 weeks (although ultrahypofractionated radiation therapy consisting of as few as 5 fractions is seeing greater adoption in the U.S.), brachytherapy can be performed in as few as 1 session using permanent seeds or 2 sessions using temporary implants.<sup>9</sup>

Brachytherapy also compares favorably to nerve sparing radical prostatectomy in terms of quality of life. In a recent prospective study of 1,386 men with favorable risk prostate cancer LDR brachytherapy had a significantly less negative impact on sexual function and urinary continence compared to nerve sparing prostatectomy, while producing more irritative urinary symptoms and worse bowel function.<sup>10</sup>

Furthermore, brachytherapy—particularly LDR brachytherapy—is a cost effective option for patients with favorable risk disease. A cost effectiveness analysis that incorporated the cost of initial treatment as well as the costs of managing adverse effects, surveillance and patient time revealed that for men age 65 years old or older the cost of brachytherapy was \$2,806 less than open prostatectomy based on a Medicare fee schedule.<sup>11</sup> A second study using time driven, activity based costing from the treatment of low risk prostate cancer estimated that through 5 years of followup LDR brachytherapy costs \$7,968 less than robotic prostatectomy.<sup>12</sup>

Modern brachytherapy is an optimal option for men with favorable risk prostate cancer and minimal baseline irritative urinary symptoms. It provides an excellent opportunity for collaboration between brachytherapists and urologists at the time of implantation and postoperative management.

Despite its advantages,

brachytherapy is sometimes not an ideal treatment option for certain patients and, therefore, patient selection is crucial. Patients with contraindications to radiation therapy including those with certain connective tissue disorders or inflammatory bowel disease should not be considered for brachytherapy. Having a prostate gland larger than 60 cc and significant obstructive urinary symptoms based on the International Prostate Symptom Score are relative contraindications to brachytherapy. These patients are at greater risk of acute urinary retention after brachytherapy, and baseline obstructive urinary symptoms would be expected to worsen in the long term. These 2 groups of patients may be better served by radical prostatectomy to relieve the obstruction. Other relative contraindications include prior pelvic radiation, a large median gland, a large transurethral resection of the prostate defect and prior rectal surgery.

Advancements in multiparametric magnetic resonance imaging (MRI) and its increasing adoption in clinical care provide an exciting opportunity for prostate brachytherapy. There is significant interest in the incorporation of MRI, either obtained as part of the diagnostic evaluation or dedicated imaging at the time of implantation, into the treatment planning process to increase the precision of the radioisotope placement. Risk adaptive strategies when higher doses are delivered to the primary lesions within the gland as identified on MRI compared to the rest of the gland are being actively investigated.<sup>13</sup> Additionally, interest in partial gland brachytherapy via identification

▼ Continued on page 10

FROM THE *AUA Secretary***Actions and Updates from the Winter AUA Board of Directors Meeting**

**John D. Denstedt, MD,  
FRCSC, FACS, FCAHS**  
London, Ontario, Canada

Listed below are several action items and updates from the February 2020 meeting of the AUA Board of Directors.

**AUA President-Elect Confirmed**

Dr. Raju Thomas will serve as the AUA President-Elect from May 2020-2021 to then ascend to AUA President from May 2021-2022. Dr. Thomas is chair of the Department of Urology at Tulane University Medical Center. His career has been dedicated to finding minimally invasive

therapy alternatives to open urological surgery. He has the distinction of introducing laparoscopy to urology in 1991, and in 2002 was the first surgeon to perform robotic surgery in the entire Gulf South. Dr. Thomas has authored more than 180 scientific articles and book chapters, and was the recipient of the AUA Distinguished Service Award in 2016.

**New AUA Education Council Chair**

Dr. Jay D. Raman of Penn State Health has been appointed by the AUA Board of Directors as the new chair-elect of the AUA Office of Education beginning June 1, 2020 and will start the 4-year term as chair on June 1, 2021. He will lead the AUA Education Council, providing

strategic oversight to shape and execute the education initiatives of the AUA. During the last 10 years Dr. Raman has served as faculty for more than 20 AUA courses, director for the Fundamentals in Urology Course, chair of the Urology Video Education Committee and member of the AUA Education Council. He currently is the Mid-Atlantic Section representative on the Editorial Board of *The Journal of Urology*®.

**AUA University YouTube Channel Update**

In May 2019 the AUA Office of Education launched the AUA University YouTube Channel. The channel features a wide variety of educational videos, as well as all of the podcasts. AUA members now have access to free urological education right at their fingertips. The YouTube Channel has nearly 400 subscribers and more than 16,300 views.

**New AUA Guideline Topic**

The AUA Board of Directors approved the topic of upper tract urothelial carcinoma for a new guideline to be developed in the next 18 months. Upper tract urothelial carcinoma is a topic that has been continually proposed by AUA membership because it is a disease associated with significant morbidity and poor prognosis.

**Urology Care Foundation Humanitarian Grant Program**

The new Urology Care Foundation Humanitarian Grant Program will recognize and support individuals and projects that provide direct urology care to impoverished individuals and communities in underserved areas either in the United States or abroad. Grants will be given to AUA members who are pursuing significant and outstanding contributions to humanitarian urological efforts in improving patient care. See page 15 in the April issue of *AUANEWS* for more information about this program. ♦

FROM THE *AUA Public Policy Council***Remembering the “Why” of Urology**

**Christopher M.  
Gonzalez, MD, MBA**  
Chair, AUA Public  
Policy Council  
Chicago, Illinois

As my service with AUA Public Policy ends I am reminded of the book *Start with Why* by Simon Sinek.<sup>1</sup> The book explains that the best organizations inspire their members with “why” they exist as compared to “how” or “what” they do.

According to our mission statement, the AUA promotes the highest standards of urological clinical care through education, research and the formulation of health care policy. In simple terms the AUA’s “why” is the support and protection of our ability to provide the best care possible for our patients.

To this end, the AUA Public Policy Council identifies the ongoing threats to our practice and formulates plans to mitigate those threats independently or through

coalitions within or outside our specialty. Examples of successful public policy victories to preserve practice include the U.S. Preventive Services Task Force recommendation change from a D to a C to restore appropriate prostate cancer screening, state by state defeat of legislation designed to restrict and/or ban the care we provide to our pediatric intersex patients, and the establishment of fair reimbursement for the revised evaluation and management urology codes.

As the number of threats has grown, recent AUA public policy expansion has met these challenges. The formation of the State Advocacy Committee has allowed us to mitigate and defeat harmful legislation at the local level while the Patient Advocacy Program has provided high level patient engagement and effective advocacy efforts with lawmakers. The Research Advocacy Committee has provided vision and strategy to heighten our presence at the National Institutes of Health and with Congress to promote the importance of research funding for

urological diseases. The regulatory and workforce work groups have provided analysis, strategy and communication surrounding the rapidly evolving regulatory burdens and changing membership demographics of our specialty.

Most recently, the Telehealth Task Force has provided outstanding analysis, solutions and guidance for members as they navigate through the COVID-19 crisis. Engagement of our students, trainees and recent graduates in the public policy space is one of the most important priorities for the AUA. I am happy to say that identification and training of the next generation of AUA public policy leaders continue to thrive through the Gallagher scholarship, the newly formed AUA Policy and Advocacy Resident workgroup and the H. Logan Holtgrewe fellowship training program.

The most exciting development from the last 4 years has been the establishment of the AUA Public Action Committee (AUAPAC) and the launch of the Annual Urology Advocacy Summit. The AUAPAC provides a mechanism for all urologists to get involved in the political process and advocate for

fair reimbursement, less regulatory burden, increased research dollars for urological diseases, augmentation of graduate medical training funds and medical malpractice reform.

The Summit provides the venue for the “House of Urology” to gather and advocate for these issues in Washington, D.C. every year. The 2020 Summit will be held August 31–September 2.

It has been an honor to serve AUA members, leadership and most importantly patients for the past 8 years. I want to acknowledge and thank all of the committee members on the AUA Public Policy Council, AUA staff, American Association of Clinical Urologists, Large Urology Group Practice Association leadership as well as more than a dozen urology specialty societies that partner with us on advocacy for the wonderful work they do. Congratulations to our new chair, Dr. Eugene Rhee and a heartfelt thanks to our outstanding chief policy officer Dr. Kathy Shanley for the fantastic work she does. The future is bright for our organization. ♦

1. Sinek S: *Start with Why*. New York, New York: Portfolio 2011.

## Brachytherapy Monotherapy

▼ Continued from page 8

of the dominant lesions on MRI is ongoing, which would provide the advantage of sparing treatment to segments of the gland without disease and hence a theoretical decrease in side effects.<sup>14</sup>

For patients with low and favorable intermediate risk prostate cancer seeking definitive management, brachytherapy monotherapy is a clinically and cost effective modality with a favorable morbidity profile and multiple exciting opportunities for future growth. Rather than simply a treatment of the past, prostate brachytherapy is a treatment of the past, the

present and the future for men with favorable risk prostate cancer. ◆

1. Sanda MG, Cadeddu JA, Kirkby E et al: Clinically localized prostate cancer: AUA/ASTRO/SUO guideline. Part II: recommended approaches and details of specific care options. *J Urol* 2018; **199**: 990.
2. Bekelman JE, Rumble RB, Chen RC et al: Clinically localized prostate cancer: ASCO clinical practice guideline endorsement of an American Urological Association/American Society for Radiation Oncology/Society of Urologic Oncology Guideline. *J Clin Oncol* 2018; **JCO1800606**.
3. Gray PJ, Lin CC, Cooperberg MR et al: Temporal trends and the impact of race, insurance, and socioeconomic status in the management of localized prostate cancer. *Eur Urol* 2017; **71**: 729.
4. Zelefsky MJ, Kuban DA, Levy LB et al: Multi-institutional analysis of long-term outcome for stages T1-T2 prostate cancer treated with permanent seed implantation. *Int J Radiat Oncol Biol Phys* 2007; **67**: 327.
5. Demanes DJ, Martinez AA, Ghilezan M et al: High-dose-rate monotherapy: safe and effective brachytherapy for patients with localized prostate cancer. *Int J Radiat Oncol Biol Phys* 2011; **81**: 1286.
6. Shapiro EY, Rais-Bahrami S, Morgenstern C et al: Long-term outcomes in younger men following permanent prostate brachytherapy. *J Urol* 2009; **181**: 1665.
7. Giberti C, Chiono L, Gallo F et al: Radical retropubic prostatectomy versus brachytherapy for low-risk prostatic cancer: a prospective study. *World J Urol* 2009 **27**: 607.
8. Giberti C, Gallo F, Schenone M et al: Robotic prostatectomy versus brachytherapy for the treatment of low risk prostate cancer. *Can J Urol* 2017; **24**: 8728.
9. Morton G, McGuffin M, Chung HT et al: High dose-rate prostate brachytherapy as monotherapy: a single fraction may not be enough. *Int J Radiat Oncol Biol Phys, suppl.*, 2019; **105**: S56.
10. Hoffman KE, Penson DF, Zhao Z et al: Patient-reported outcomes through 5 years for active surveillance, surgery, brachytherapy,

or external beam radiation with or without androgen deprivation therapy for localized prostate cancer. *JAMA* 2020; **323**: 149.

11. Hayes JH, Ollendorf DA, Pearson SD et al: Observation versus initial treatment for men with localized, low-risk prostate cancer: a cost-effectiveness analysis. *Ann Intern Med* 2013; **158**: 853.
12. Laviana AA, Ilg AM, Veruttipong D et al: Utilizing time-driven activity-based costing to understand the short- and long-term costs of treating localized, low-risk prostate cancer. *Cancer* 2016; **122**: 447.
13. Gomez-Iturriga A, Casquero F, Urresola A et al: Dose escalation to dominant intraprostatic lesions with MRI-transrectal ultrasound fusion high-dose-rate prostate brachytherapy. Prospective phase II trial. *Radiother Oncol* 2016; **119**: 91.
14. Valerio M, Cerantola Y, Eggenner SE et al: New and established technology in focal ablation of the prostate: a systematic review. *Eur Urol* 2017; **71**: 17.

## FROM THE AUA Research Council

# Artificial Intelligence in Urological Research



Boris Gershman, MD



Aria F. Olumi, MD  
Chair, AUA Research Council

Boston, Massachusetts

Whether users recognize it or not, artificial intelligence powers everyday interactions with technology including speech recognition, search algorithms, smartphone cameras, social media feeds and shopping recommendations.<sup>1</sup> Although the current renaissance of artificial intelligence is still in its infancy, it holds particular promise for applications in health care including urology.

The term “artificial intelligence” is broad, and most contemporary applications leverage a specific subset of machine learning techniques called deep learning.<sup>1</sup> Whereas classical machine learning relies on fairly rigid features and models designed by hand, deep learning allows the development of flexible classification models that rely only on feeding the model raw data and corresponding class labels, allowing the model to learn patterns represented in the data (see figure).<sup>1</sup> Since deep learning models require estimation of hundreds of millions

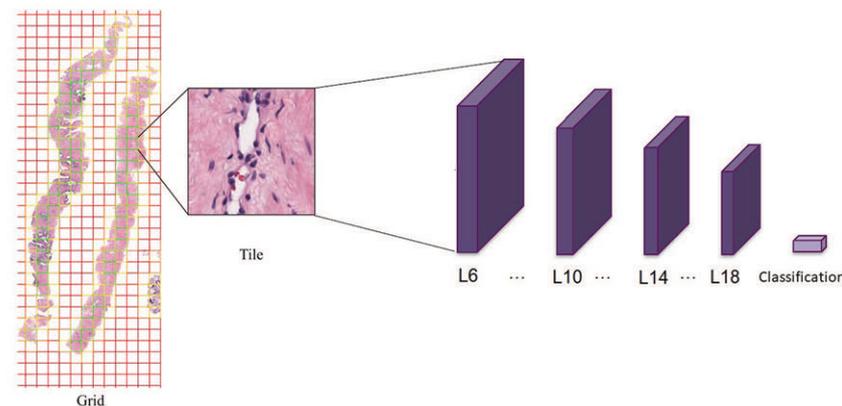
of parameters, it was not until recent advances in computer hardware and the availability of large datasets that such approaches were pragmatic for common applications.

There are already numerous high profile examples of deep learning in health care. For example, in one study a Google team developed a deep learning model to predict in-hospital mortality, 30-day readmission and even diagnoses at time of discharge with remarkable accuracy.<sup>2</sup> Notably, this effort required data from more than 200,000 patients and used more than 46 billion data points, emphasizing the scale of data required to achieve excellent performance.

In addition to clinical prediction, deep learning has been leveraged for medical image classification. By way of illustration, in the CAMELYON16 research competition, investigators developed an algorithm that detected breast cancer metastases in lymph node specimens with equal or better accuracy than a panel of 11 pathologists.

Beyond recapitulating pathological diagnosis, deep learning has also been used to predict long-term events from a radiographic study such as predicting all cause mortality from a single chest X-ray in the PLCO (Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial) study or 5-year risk of developing breast cancer from a mammogram.

Urological applications for deep



**Figure.** Illustration of workflow for processing digitized pathologic images with deep learning network. Raw source image is subdivided into image patches (left) which are then fed into 18-layer convolutional neural network (CNN). CNN then processes raw data across layers to produce final classification (eg benign vs malignant).

learning are also emerging with the majority of studies focusing on medical image classification tasks.<sup>3</sup> For instance, 2 studies recently published in *Lancet Oncology* developed deep learning algorithms for the Gleason grading of prostate biopsies and performed as well as or better than a group of reference pathologists.

Similarly, early efforts have attempted to characterize kidney tumors from cross sectional imaging. For example investigators have developed deep learning algorithms to predict kidney tumor histology from magnetic resonance imaging and multiphasic computerized tomography.<sup>3</sup> Machine learning methods that do not rely on deep learning have also been applied in attempts to improve predictive models for clinical outcomes, such as prediction of stone free rates following shockwave lithotripsy. Although much additional work is required to optimize performance and validate results, such early efforts provide examples of potential use cases in urology.

There are a number of challenges for deep learning methods in health care. Most importantly, deep learning requires large amounts of data for training to achieve optimal performance. This represents a barrier in many applications where large data sets containing raw data linked to outcomes of interest are unavailable, particularly for medical image classification tasks. Moreover, as with any predictive model deep learning models require external validation to establish realistic performance for widespread clinical applications.

Another challenge relates to dissemination. Deep learning models represent a black box. Unlike conventional models where the discrete features used for prediction are identifiable and can be understood by end users, deep learning models have no such correlate. Although methods have been described to visualize the features used by deep learning models, this truth remains a potential

▼ Continued on page 11

FROM THE *AUA Education Council*

## AUA Offers Educational Activities 24/7



**Victor W. Nitti, MD**  
Chair, AUA Education Council  
Los Angeles, California

2020 has shown us how we can and should integrate technology into our lifelong learning. Although the AUA had to cancel the 2020 annual meeting, the first time since World War II, the AUA Office of Education continues to bring you as much of that education as possible at the AUAUniversity (<https://>

[auau.auanet.org/](https://auau.auanet.org/)).

AUAUniversity is centered around a robust search engine supporting approximately 375 available activities, which allows our members to find educational content faster and more efficiently. Because our membership is diverse, with many members identifying as general urologists and others practicing within a specific patient population, the homepage offers several ways to find education. We have categorized our educational activities into the American Board of Urology Lifelong Learning categories (Core/General Urology; Oncology,

Urinary Diversion and Adrenal; Calculus, Laparoscopy-Robotics and Upper Tract Obstruction; Impotence, Infertility and Andrology; and Neurogenic Bladder, Voiding Dysfunction, Female Urinary, BPH and Urethral Stricture). The left navigation column allows you to search by those categories or alternatively by a wide variety of urological topics (eg BPH, Clinical Guidelines, Pediatrics).

Click on “Catalog” in the navigation bar at the top of the homepage to search the AUA educational library. If you are an AUA Update Series, SASP or JU Home Study subscriber, you can find these products under the “Quick Links” tab. A cornerstone of the AUAUniversity, the Core Curriculum is also easily accessible from the homepage. In the center of the homepage are the most current

course videos as well as podcasts of new, clinical episodes which are released every Wednesday.

The AUAUniversity mobile app, available on Android™ and Apple® mobile devices, is a quick, easy way to access this information on the go. From the app homepage you have direct access to all podcasts, the Core Curriculum and for subscribers, the AUA Update Series lessons and audiobooks.

If it has been a while since you visited AUAUniversity, your login has not changed. If you have any issues, please contact the AUA Customer Service Department by phone (800-908-9414 or 410-689-3917) or email ([customerservice@auanet.org](mailto:customerservice@auanet.org)). The AUAUniversity is your home for all AUA live and home study activities 24/7. Check it out! ♦

### From the AUA Research Council

▼ Continued from page 10

barrier to adoption.

Ethical issues will also need to be addressed. For instance, deep learning algorithms may promote racial bias and discrimination inherent in nonrepresentative training data. Conversely, it is possible that a diversely trained algorithm may be less subject to such racial bias than existing clinical models, as was observed in a study that compared deep learning and clinical models for predicting breast cancer risk. Furthermore, recent expansion of privacy regulations such as the General Data Protection Regulation (GDPR) in Europe will make the creation of large datasets for deep learning applications more challenging.

Despite these challenges, artificial intelligence holds tremendous promise for accelerating advances and paradigmatic shifts in health care. While the ultimate impact on patient care will depend on many factors, it represents an exciting opportunity for urologists to lead in technological innovation and address key issues related to data availability, patient privacy and ethics. ♦

1. LeCun Y, Bengio Y and Hinton G: Deep learning. *Nature* 2015; **521**: 436.
2. Rajkomar A, Oren E, Chen K et al: Scalable and accurate deep learning with electronic health records. *NPJ Digit Med* 2018; **1**: 18.
3. Suarez-Ibarrola R, Hein S, Reis G et al: Current and future applications of machine and deep learning in urology: a review of the literature on urolithiasis, renal cell carcinoma, and bladder and prostate cancer. *World J Urol* 2019; doi:10.1007/s00345-019-03000-5.

# WE ARE COUNTING ON YOU TO MAKE A DIFFERENCE!

## TAKE THE 2020 AUA | ANNUAL CENSUS

[AUAnet.org/TakeCensus](https://AUAnet.org/TakeCensus)



American  
Urological  
Association

Advancing Urology™

## CASE Report

# Primary Emphysematous Spermatic Cord Abscess with Seminal Vesiculitis in a Diabetic Man



Akash Bansal, MD



Pankaj Agarwal, MD



Apul Goel, MD

Lucknow, India

A 49-year-old man presented with mildly painful swelling in the right groin along with intermittent fever 6 days in duration. He denied vomiting and urinary complaints, and bladder and bowel habits were normal. Temperature was 37.9 C, blood pressure 112/76 mm Hg, pulse 95 beats per minute and respiration 20 breaths per minute.

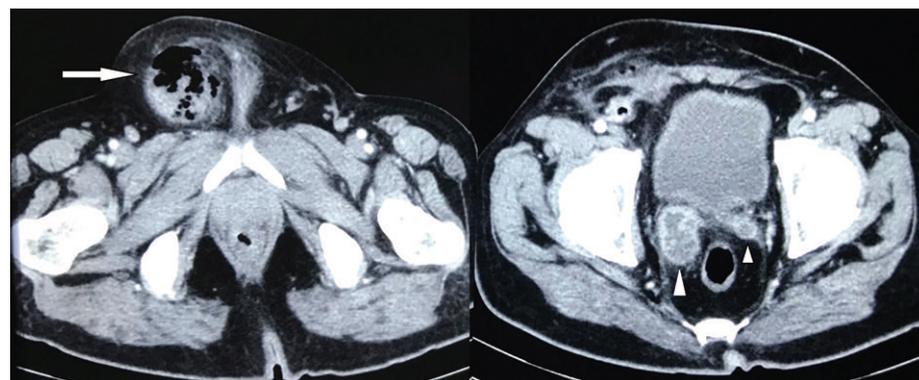
Examination revealed a tender, irreducible, nonpulsatile mass approximately 4 cm in diameter in the

right inguinal scrotal region that did not increase with Valsalva maneuver. The overlying skin, scrotum and testicles showed no signs of inflammation (fig. 1). All laboratory tests were unremarkable except for leukocytosis ( $13,500/\text{mm}^3$ ), and elevated blood sugars (380 mg/dl) and glycosylated hemoglobin (12.8%). Diagnosis was diabetes mellitus.

Further evaluation with ultrasonography and computerized tomography (CT) suggested a diagnosis of



**Figure 1.** A, right emphysematous spermatic cord abscess. B, intraoperative image shows right inguinal skin incision with tense cystic mass of right spermatic cord prior to incision and drainage (arrow), and scrotum (arrowhead). C, intraoperative image after incision of abscess reveals vacuum suction draining thick pus with air bubbles (arrow) and scrotum (arrowhead).



**Figure 2.** Axial CT shows pus collection with air foci in right spermatic cord within inguinal canal and right hemiscrotum (arrow), and bilateral enlarged seminal vesicles (more on right side) with heterogeneous enhancement (arrowhead).

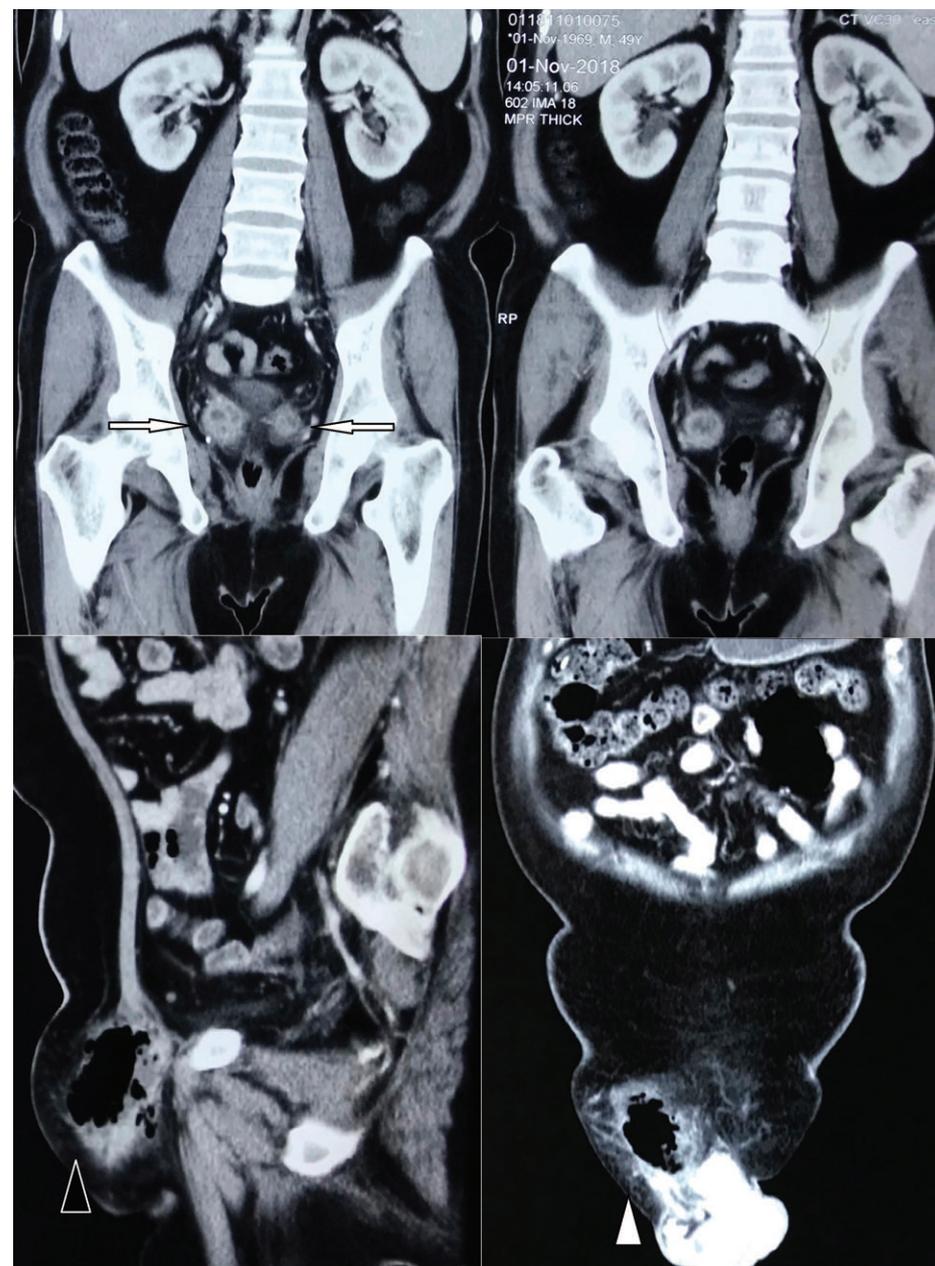
right emphysematous spermatic cord abscess with right epididymitis and seminal vesiculitis (figs. 2 and 3). Inguinal exploration was performed during which division of the cremaster muscle revealed an oval encapsulated 4 cm mass filled with pus. The mass was incised and the abscess with air bubbles was drained.

Initially, empirical antibiotic therapy was started followed by antibiotic administration based on the culture sensitivity report. *Escherichia*

*coli* was cultured from the pus. Convalescence was uneventful and the patient was afebrile at the time he was discharged home. Ultrasound at 3-month followup revealed complete healing of the wound and uroflowmetry was normal.

Gas forming or emphysematous pathology is a potentially life-threatening condition that necessitates prompt assessment and management.

▼ Continued on page 13



**Figure 3.** CT shows bilateral enlarged seminal vesicles with heterogeneous enhancement suggestive of seminal vesiculitis in coronal section (arrows) and thickened edematous right spermatic cord containing pus and multiple air foci within inguinal canal and right hemiscrotum (black arrowhead, sagittal section; white arrowhead, coronal section).

## Emphysematous Spermatic Cord Abscess

▼ Continued from page 12

Immediate therapeutic intervention is required to avoid septic complications. Besides infection, the causes of air within the parenchyma of solid organs or the walls of hollow viscera are instrumentation, fistula to a hollow viscus and tissue infarction with necrosis.<sup>1</sup> Gas associated with infection consists of carbon dioxide and nitrogen that is produced secondary to fermentation of tissue glucose by certain species of bacteria.<sup>1</sup>

Emphysematous infections are relatively uncommon and cases have been reported in the literature<sup>1</sup> involving the gallbladder, pancreas, stomach, kidney,<sup>2</sup> and bladder<sup>3</sup> as well as the genital tracts including the prostate, epididymis, testis<sup>4,6</sup> and rarely

the spermatic cord.<sup>7</sup> Approximately 90% of these infections occur in diabetic patients. The route of infection is usually hematogenous.

The primary factors considered vital in the development of any emphysematous infection are gas forming bacteria that vary depending on the organ involved. In the genitourinary tract the most common isolated organism is *E. coli* whereas in the gastrointestinal tract isolated organisms commonly include *Clostridium welchii* and *E. coli*.<sup>1</sup> Other organisms that have been isolated in various emphysematous infections are *Klebsiella pneumoniae*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Enterobacter aerogenes*, *Staphylococcus aureus*, streptococcus, *Clostridium perfringens* and *Candida albicans*.<sup>2,3</sup>

Other factors responsible for the

development of emphysematous infection include high tissue glucose levels, decreased tissue perfusion and an inadequate immune response.<sup>2</sup> Apart from antimicrobial therapy and need for surgery, correction of associated underlying conditions such as urinary outflow obstruction, acid/base and electrolyte imbalances, hypovolemia and hyperglycemia is imperative.<sup>1</sup>

In the genitourinary tract literature emphysematous infection of the spermatic cord has rarely been reported. To our knowledge, only 1 case of emphysematous vasitis has been reported in the literature which was associated with diabetes mellitus and rectal cancer, and managed with left spermatic cord excision.<sup>7</sup> We present another rare case of emphysematous spermatic cord abscess with diabetes mellitus. ♦

1. Grayson DE, Abbott RM, Levy AD et al: Emphysematous infections of the abdomen and pelvis: a pictorial review. *Radiographics* 2002; **22**: 543.
2. Ubee SS, McGlynn L and Fordham M: Emphysematous pyelonephritis. *BJU Int* 2011; **107**: 1474.
3. Fumeo M, Manfredi S and Volta A: Emphysematous cystitis: review of current literature, diagnosis and management challenges. *Vet Med (Auckl)* 2019; **10**: 77.
4. Mathur A, Manish A, Maletha M et al: Emphysematous epididymo-orchitis: a rare entity. *Indian J Urol* 2011; **27**: 399.
5. Yen CH, Liu CY, Cha TL et al: Emphysematous epididymo-orchitis as a camouflage of prostate invasion secondary to rectum cancer: a case report. *Medicine (Baltimore)* 2016; **95**: e4385.
6. Lau HW, Yu CH, Yu SM et al: Emphysematous epididymo-orchitis: an uncommon but life-threatening cause of scrotal pain. *Hong Kong Med J* 2018; **24**: 426.
7. You SH, Sung DJ, Han NY et al: Emphysematous vasitis misdiagnosed as strangulated inguinal hernia. *J Emerg Med* 2014; **47**: e15.

## Botulinum Neurotoxin for Sexual Dysfunction



Brian Dick, MD



Bryan Herzog, MD



Wayne J. G. Hellstrom, MD, FACS

New Orleans, Louisiana

Botulinum neurotoxin (BoNT) was first identified in the late 1800s as the causative paralytic agent in patients with botulism syndrome. It was discovered that BoNT acts at the presynaptic terminal to prevent exocytosis of acetylcholine (ACh), resulting in a flaccid paralysis.

Newer research has revealed that BoNT also inhibits exocytosis of neuropeptides associated with neuropathic pain, including substance P (SP) and calcitonin gene related peptide (CGRP). Several studies report a direct analgesic effect of BoNT at the site of injection, although the physiological mechanism has not been fully elucidated.<sup>1</sup> It is through these mechanisms that BoNT is hypothesized to treat a variety of sexual dysfunctions in men and women.

Chronic scrotal pain (CSP) is a burdensome condition that interferes with lives in a profound way. It is defined throughout the literature as intermittent or constant unilateral or bilateral testicular pain present for

more than 3 months. Besides antibiotics and spermatic cord blockade, there are few noninvasive treatment options. During the last several years BoNT injection has been identified as a novel noninvasive approach with promise as a treatment alternative.

BoNT is hypothesized to decrease the release of SP and CGRP, thus leading to inhibition of neurogenic inflammation and pain.<sup>2</sup> Of 44 patients treated for CSP with BoNT injections pain resolved completely in 7.5% and decreased by more than 50% in 55% with no reported side effects or complications at a median followup of 6 months. This duration of pain relief from a single administration of BoNT is significantly longer than the few hours of pain relief provided by a standard spermatic cord block.

BoNT is also postulated to aid patients who suffer from erectile dysfunction (ED). It inhibits the adrenergic and cholinergic nerve pathways. In the adrenergic pathway BoNT blocks the release of norepinephrine

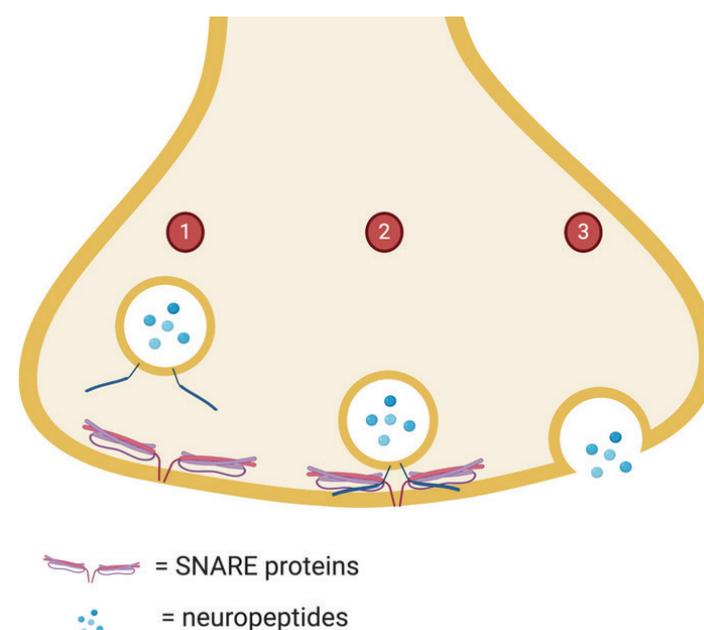
from sympathetic neurons, thereby inhibiting cavernosal muscle contraction. In the cholinergic pathway it blocks ACh release from cholinergic neurons preventing cavernosal muscle relaxation, suggesting that the cavernosal muscle relaxation observed after BoNT administration is mediated by the release of neuronal nitric oxide from nonadrenergic, noncholinergic neurons.

In a clinical trial 24 men with severe vasculogenic ED refractory to phosphodiesterase 5 inhibitors received intracavernosal injections of BoNT. The treatment group experienced increases in mean peak systolic velocity from 24.6 cm per second to 34.9 cm per second, mean Sexual Health Inventory for Men score from 5.58 to 10.25 ( $p=0.0075$ ) and mean

Erection Hardness Score from 2 to 2.75.<sup>3</sup>

BoNT has also been demonstrated to treat premature ejaculation (PE), a male sexual dysfunction characterized by ejaculation that always or nearly always occurs before or within 1 minute of vaginal penetration. It is known that rhythmic contraction of the bulbospongiosus muscles plays a role in ejaculation. BoNT injection into the bulbospongiosus muscles is believed to prevent PE by decreasing these rhythmic contractions and causing a delay in the ejaculatory process.

Of 69 patients with PE 34 received BoNT injections into the bulbospongiosus muscles.<sup>4</sup> At 4 weeks



**Figure 1.** Healthy presynaptic neuron. 1, Neuropeptides (ACh, SP, CGRP etc) are stored in vesicles in presynaptic terminal. 2, Vesicle attaches to presynaptic membrane via interactions between SNARE proteins. 3, Vesicle fuses with presynaptic membrane, releasing neuropeptides into synapse.

▼ Continued on page 19

**For your adult patients with overactive bladder (OAB) symptoms of urge urinary incontinence, urgency, and urinary frequency...**



It's time to address his OAB symptoms

**He has places to go.**

**Myrbetriq<sup>®</sup> (mirabegron) is the first and only FDA-approved  $\beta_3$ -adrenergic agonist. Myrbetriq is indicated for the treatment of OAB with symptoms of urge urinary incontinence, urgency, and urinary frequency.**

- **Safety and efficacy evaluated in elderly patients**

No overall differences in safety or effectiveness were observed between patients <65 years and those  $\geq$ 65 years of age in the Phase II and III studies of Myrbetriq. Of the 5648 patients who received Myrbetriq in the Phase II and III studies, 2029 (35.9%) were  $\geq$ 65 years of age, and 557 (9.9%) were  $\geq$ 75 years of age.<sup>1</sup>

- **No dose adjustments needed for the elderly<sup>1</sup>**

- **Similar pharmacokinetics**

The pharmacokinetics of Myrbetriq were similar in elderly and younger volunteers<sup>1</sup>

- **Prospective Phase IV PILLAR trial published February 2020**

This double-blind, randomized, 12-week study evaluated the safety and efficacy of flexibly-dosed Myrbetriq vs. placebo in community-dwelling patients  $\geq$ 65 years of age with OAB symptoms. Entry criteria required symptoms of wet OAB for  $\geq$ 3 months with  $\geq$ 1 incontinence episode,  $\geq$ 3 urgency episodes, and an average of  $\geq$ 8 micturition episodes/day based on a 3-day micturition diary.<sup>2</sup> The study's endpoints included:

- **Incontinence episodes**

Primary endpoint: change from baseline to end of treatment (EoT) in mean number of urinary incontinence episodes per 24 hours

- **Frequency**

Primary endpoint: change from baseline to EoT in mean number of urinary incontinence episodes per 24 hours

- **Volume voided per micturition**

Secondary endpoint: change from baseline to EoT in mean volume voided per micturition

#### **INDICATIONS AND USAGE**

Myrbetriq<sup>®</sup> (mirabegron) is a beta-3 adrenergic agonist indicated for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency.

#### **IMPORTANT SAFETY INFORMATION**

Do not use Myrbetriq in patients who have known hypersensitivity reactions to mirabegron or any component of the tablet.



Visit [www.MyrbetriqPILLAR.com](http://www.MyrbetriqPILLAR.com)  
to learn more about the PILLAR trial

### IMPORTANT SAFETY INFORMATION (cont'd)

Myrbetriq can increase blood pressure. Periodic blood pressure determinations are recommended, especially in hypertensive patients. Myrbetriq is not recommended for use in severe uncontrolled hypertensive patients (defined as systolic blood pressure  $\geq 180$  mm Hg and/or diastolic blood pressure  $\geq 110$  mm Hg). Worsening of hypertension was reported infrequently in Myrbetriq clinical trial patients with OAB.

In patients taking Myrbetriq, urinary retention has been reported in patients with bladder outlet obstruction (BOO) and in patients taking antimuscarinic medications for the treatment of OAB. A controlled clinical safety study in patients with BOO did not demonstrate increased urinary retention in Myrbetriq patients; however, Myrbetriq should still be administered with caution to patients with clinically significant BOO. For example, monitor these patients for signs and symptoms of urinary retention. Myrbetriq should also be administered with caution to patients taking antimuscarinic medications for the treatment of OAB.

Angioedema of the face, lips, tongue and/or larynx has been reported with Myrbetriq. In some cases angioedema occurred after the first dose. Cases of angioedema have been reported to occur hours after the first dose or after multiple doses. Angioedema associated with upper airway swelling may be life threatening. If involvement of the tongue, hypopharynx, or larynx occurs, promptly discontinue Myrbetriq and initiate appropriate therapy and/or measures necessary to ensure a patent airway.

Since Myrbetriq is a moderate CYP2D6 inhibitor, the systemic exposure to CYP2D6 substrates such as metoprolol and desipramine is increased when co-administered with Myrbetriq. Appropriate monitoring and dose adjustment may be necessary, especially with narrow therapeutic index drugs metabolized by CYP2D6, such as thioridazine, flecainide, and propafenone.

In clinical trials, the most commonly reported adverse reactions ( $> 2\%$  and  $>$  placebo) for Myrbetriq 25 mg and 50 mg versus placebo, respectively, were hypertension (11.3%, 7.5% vs 7.6%), nasopharyngitis (3.5%, 3.9% vs 2.5%), urinary tract infection (4.2%, 2.9% vs 1.8%), and headache (2.1%, 3.2% vs 3.0%).

In postmarketing experience, the following events have also occurred: atrial fibrillation, nausea, constipation, diarrhea, and dizziness.

**Please see accompanying brief summary of Prescribing Information for Myrbetriq® (mirabegron) on the following pages.**

**References:** 1. Myrbetriq [package insert]. Northbrook, IL: Astellas Pharma US, Inc. 2. Wagg A, Staskin D, Engel E, Herschorn S, Kristy RM, Schermer CR. Efficacy, safety, and tolerability of mirabegron in patients aged  $\geq 65$  yr with overactive bladder wet: a phase IV, double-blind, randomized, placebo-controlled study (PILLAR). *Eur Urol* 2020;77(2):211-20.

## BRIEF SUMMARY OF PRESCRIBING INFORMATION

The following information is a brief summary only. See full prescribing information for MYRBETRIQ®.

### MYRBETRIQ (mirabegron) extended-release tablets

#### INDICATIONS AND USAGE

MYRBETRIQ® is a beta-3 adrenergic agonist indicated for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency.

#### CONTRAINDICATIONS

Do not use MYRBETRIQ in patients who have known hypersensitivity reactions to mirabegron or any component of the tablet.

#### WARNINGS AND PRECAUTIONS

##### Increases in Blood Pressure

MYRBETRIQ can increase blood pressure. Periodic blood pressure determinations are recommended, especially in hypertensive patients. MYRBETRIQ is not recommended for use in patients with severe uncontrolled hypertension (defined as systolic blood pressure greater than or equal to 180 mm Hg and/or diastolic blood pressure greater than or equal to 110 mm Hg).

In two, randomized, placebo-controlled, healthy volunteer studies, MYRBETRIQ was associated with dose-related increases in supine blood pressure. In these studies, at the maximum recommended dose of 50 mg, the mean maximum increase in systolic/diastolic blood pressure was approximately 3.5/1.5 mm Hg greater than placebo.

In contrast, in OAB patients in clinical trials, MYRBETRIQ taken as monotherapy, the mean increase in systolic and diastolic blood pressure at the maximum recommended MYRBETRIQ dose of 50 mg was approximately 0.5 to 1 mm Hg greater than placebo. Worsening of pre-existing hypertension was reported infrequently in MYRBETRIQ patients.

##### Urinary Retention in Patients with Bladder Outlet Obstruction and in Patients Taking Muscarinic Antagonist Medications for OAB

In patients taking MYRBETRIQ, urinary retention has been reported to occur in patients with bladder outlet obstruction (BOO) and in patients taking muscarinic antagonist medications for the treatment of OAB. A controlled clinical safety study in patients with BOO did not demonstrate increased urinary retention in MYRBETRIQ patients; however, MYRBETRIQ should still be administered with caution to patients with clinically significant BOO. For example, monitor these patients for signs and symptoms of urinary retention. MYRBETRIQ should also be administered with caution to patients taking muscarinic antagonist medications for the treatment of OAB, including solifenacin succinate.

##### Angioedema

Angioedema of the face, lips, tongue, and/or larynx has been reported with MYRBETRIQ. In some cases angioedema occurred after the first dose. Cases of angioedema have been reported to occur hours after the first dose or after multiple doses. Angioedema associated with upper airway swelling may be life threatening. If involvement of the tongue, hypopharynx, or larynx occurs, promptly discontinue MYRBETRIQ and initiate appropriate therapy and/or measures necessary to ensure a patent airway.

##### Patients Taking Drugs Metabolized by CYP2D6

Since mirabegron is a moderate CYP2D6 inhibitor, the systemic exposure to CYP2D6 substrates such as metoprolol and desipramine is increased when co-administered with mirabegron. Therefore, appropriate monitoring and dose adjustment may be necessary, especially with narrow therapeutic index drugs metabolized by CYP2D6, such as thioridazine, flecainide, and propafenone.

#### ADVERSE REACTIONS

##### Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

In three, 12-week, double-blind, placebo-controlled, safety and efficacy studies in patients with overactive bladder (Studies 1, 2, and 3), MYRBETRIQ was evaluated for safety in 2736 patients. Study 1 also included an active control. For the combined Studies 1, 2, and 3, 432 patients received MYRBETRIQ 25 mg, 1375 received MYRBETRIQ 50 mg, and 929 received MYRBETRIQ 100 mg once daily. In these studies, the majority of the patients were Caucasian (94%), and female (72%) with a mean age of 59 years (range 18 to 95 years).

MYRBETRIQ was also evaluated for safety in 1632 patients who received MYRBETRIQ 50 mg once daily (n=812 patients) or MYRBETRIQ 100 mg (n=820 patients) in a 1 year, randomized, fixed dose, double-blind, active controlled, safety study in patients with overactive bladder (Study 4). Of these patients, 731 received MYRBETRIQ in a previous 12-week study. In Study 4, 1385 patients received MYRBETRIQ continuously for at least 6 months, 1311 patients received MYRBETRIQ for at least 9 months, and 564 patients received MYRBETRIQ for at least 1 year.

The most frequent adverse events (0.2%) leading to discontinuation in Studies 1, 2 and 3 for the 25 mg or 50 mg dose were nausea, headache, hypertension, diarrhea, constipation, dizziness and tachycardia.

Atrial fibrillation (0.2%) and prostate cancer (0.1%) were reported as serious adverse events by more than 1 patient and at a rate greater than placebo.

Table 1 lists adverse reactions, derived from all adverse events, that were reported in Studies 1, 2 and 3 at an incidence greater than placebo and in 1% or more of patients treated with MYRBETRIQ 25 mg or 50 mg once daily for up to 12 weeks. The most commonly reported adverse reactions (greater than 2% of MYRBETRIQ patients and greater than placebo) were hypertension, nasopharyngitis, urinary tract infection and headache.

**Table 1: Percentages of Patients with Adverse Reactions, Derived from All Adverse Events, Exceeding Placebo Rate and Reported by 1% or More of Patients Treated with MYRBETRIQ 25 mg or 50 mg Once Daily in Studies 1, 2, and 3**

	Placebo (%)	MYRBETRIQ 25 mg (%)	MYRBETRIQ 50 mg (%)
<b>Number of Patients</b>	<b>1380</b>	<b>432</b>	<b>1375</b>
Hypertension*	7.6	11.3	7.5
Nasopharyngitis	2.5	3.5	3.9
Urinary Tract Infection	1.8	4.2	2.9
Headache	3.0	2.1	3.2
Constipation	1.4	1.6	1.6
Upper Respiratory Tract Infection	1.7	2.1	1.5
Arthralgia	1.1	1.6	1.3
Diarrhea	1.3	1.2	1.5
Tachycardia	0.6	1.6	1.2
Abdominal Pain	0.7	1.4	0.6
Fatigue	1.0	1.4	1.2

\*Includes reports of blood pressure above the normal range, and BP increased from baseline, occurring predominantly in subjects with baseline hypertension.

Other adverse reactions reported by less than 1% of patients treated with MYRBETRIQ in Studies 1, 2, or 3 included:

*Cardiac disorders:* palpitations, blood pressure increased

*Eye disorders:* glaucoma

*Gastrointestinal disorders:* dyspepsia, gastritis, abdominal distension

*Infections and Infestations:* sinusitis, rhinitis

*Investigations:* GGT increased, AST increased, ALT increased, LDH increased

*Renal and urinary disorders:* nephrolithiasis, bladder pain

*Reproductive system and breast disorders:* vulvovaginal pruritus, vaginal infection

*Skin and subcutaneous tissue disorders:* urticaria, leukocytoclastic vasculitis, rash, pruritus, purpura, lip edema

Table 2 lists the rates of the most commonly reported adverse reactions, derived from all adverse events in patients treated with MYRBETRIQ 50 mg for up to 52 weeks in Study 4. The most commonly reported adverse reactions (> 3% of MYRBETRIQ patients) were hypertension, urinary tract infection, headache, and nasopharyngitis.

**Table 2: Percentages of Patients with Adverse Reactions, Derived from All Adverse Events, Reported by Greater Than 2% of Patients Treated with MYRBETRIQ 50 mg Once Daily in Study 4**

	MYRBETRIQ 50 mg (%)	Active Control (%)
<b>Number of Patients</b>	<b>812</b>	<b>812</b>
Hypertension	9.2	9.6
Urinary Tract Infection	5.9	6.4
Headache	4.1	2.5
Nasopharyngitis	3.9	3.1
Back Pain	2.8	1.6
Constipation	2.8	2.7
Dry Mouth	2.8	8.6
Dizziness	2.7	2.6
Sinusitis	2.7	1.5
Influenza	2.6	3.4
Arthralgia	2.1	2.0
Cystitis	2.1	2.3

In Study 4, in patients treated with MYRBETRIQ 50 mg once daily, adverse reactions leading to discontinuation reported by more than 2 patients and at a rate greater than active control included: constipation (0.9%), headache (0.6%), dizziness (0.5%), hypertension (0.5%), dry eyes (0.4%), nausea (0.4%), vision blurred (0.4%), and urinary tract infection (0.4%). Serious adverse events reported by at least 2 patients and exceeding active control included cerebrovascular accident (0.4%) and osteoarthritis (0.2%). Serum ALT/AST increased from baseline by greater than 10-fold in 2 patients (0.3%) taking MYRBETRIQ 50 mg, and these markers subsequently returned to baseline while both patients continued MYRBETRIQ.

In Study 4, serious adverse events of neoplasm were reported by 0.1%, 1.3%, and 0.5% of patients treated with MYRBETRIQ 50 mg, MYRBETRIQ 100 mg and active control once daily, respectively. Neoplasms reported by 2 patients treated with MYRBETRIQ 100 mg included breast cancer, lung neoplasm malignant and prostate cancer. A causal relationship between mirabegron and these reported neoplasms has not been established.

In a separate clinical study in Japan, a single case was reported as Stevens-Johnson syndrome with increased serum ALT, AST and bilirubin in a patient taking MYRBETRIQ 100 mg as well as an herbal medication (Kyufu Gold).

#### Postmarketing Experience

The following adverse reactions have been identified during post-approval use of mirabegron. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. The following events have been reported in association with mirabegron use in worldwide postmarketing experience: *Cardiovascular disorders: atrial fibrillation*

*Gastrointestinal disorders: nausea, constipation, diarrhea*

*Nervous system disorders: dizziness, headache*

There have been postmarketing reports of confusion, hallucinations, insomnia and anxiety in patients taking mirabegron. The majority of these patients had pre-existing medical conditions or concomitant medications that may cause confusion, hallucinations, insomnia and anxiety. A causal relationship between mirabegron and these disorders has not been established.

*Skin and subcutaneous tissue: angioedema of the face, lips, tongue, and larynx, with or without respiratory symptoms; pruritus*

*Urologic: urinary retention*

#### -----DRUG INTERACTIONS-----

Drug interaction studies were conducted to investigate the effect of co-administered drugs on the pharmacokinetics of mirabegron and the effect of mirabegron on the pharmacokinetics of co-administered drugs (e.g., ketoconazole, rifampin, solifenacin, tamsulosin, and oral contraceptives). No dose adjustment is recommended when these drugs are co-administered with mirabegron.

The following are drug interactions for which monitoring is recommended:

#### Drugs Metabolized by CYP2D6

Since mirabegron is a moderate CYP2D6 inhibitor, the systemic exposure of drugs metabolized by CYP2D6 enzyme such as metoprolol and desipramine is

increased when co-administered with mirabegron. Therefore, appropriate monitoring and dose adjustment may be necessary when MYRBETRIQ is co-administered with these drugs, especially with narrow therapeutic index CYP2D6 substrates, such as thioridazine, flecainide, and propafenone.

#### Digoxin

When given in combination, mirabegron increased mean digoxin  $C_{max}$  from 1.01 to 1.3 ng/mL (29%) and AUC from 16.7 to 19.3 ng.h/mL (27%). For patients who are initiating a combination of mirabegron and digoxin, the lowest dose for digoxin should initially be considered. Serum digoxin concentrations should be monitored and used for titration of the digoxin dose to obtain the desired clinical effect.

#### Warfarin

The mean  $C_{max}$  of S- and R-warfarin was increased by approximately 4% and AUC by approximately 9% when administered as a single dose of 25 mg after multiple doses of 100 mg mirabegron. Following a single dose administration of 25 mg warfarin, mirabegron had no effect on the warfarin pharmacodynamic endpoints such as International Normalized Ratio (INR) and prothrombin time. However, the effect of mirabegron on multiple doses of warfarin and on warfarin pharmacodynamic end points such as INR and prothrombin time has not been fully investigated.

#### -----USE IN SPECIFIC POPULATIONS-----

#### Pregnancy

##### Risk Summary

There are no studies with the use of MYRBETRIQ in pregnant women to inform drug-associated risk for birth defects or miscarriage. Mirabegron administration to pregnant animals during organogenesis resulted in reversible skeletal variations (in rats) at 22-fold (via AUC) the maximum recommended human dose (MRHD) of 50 mg/day and decreased fetal body weights (in rabbits) at 14-fold the MRHD. At maternally toxic exposures in rats (96-fold), decreased fetal weight and increased fetal mortality were observed and, in rabbits (36-fold), cardiac findings (fetal cardiomegaly and fetal dilated aortae) were observed.

The estimated background risks of major birth defects and miscarriage for the indicated populations are unknown. In the U.S. general population, the estimated background risks of major birth defects and miscarriage in clinically recognized pregnancies are 2-4% and 15-20%, respectively.

##### Data

##### Animal Data

No embryo-fetal lethality or morphological fetal developmental abnormalities were produced in pregnant rats following daily oral administration of mirabegron during the period of organogenesis (Days 7 to 17 of gestation) at 0, 10, 30, 100, or 300 mg/kg, doses which were associated with systemic exposures (AUC) 0, 1, 6, 22 and 96-fold the MRHD. Skeletal variations (wavy ribs, delayed ossification) were observed in fetuses at doses 22-fold the systemic exposure at the MRHD and were reversible during development. Exposures 96-fold the MRHD were maternally toxic (mortality, decreased body weight gain) and associated with fetal growth reduction.

Pregnant rabbits were treated with daily oral doses of mirabegron at 0, 3, 10, or 30 mg/kg/day during the period of organogenesis (Days 6 to 20 of gestation), which resulted in plasma exposures that were 0, 1, 14, or 36-fold the MRHD based on AUC. At 10 mg/kg/day (14-fold the MRHD) and higher, fetal body weights were reduced. At 30 mg/kg/day, maternal toxicity (increased heart rate, mortality, reduced body weight gain, reduced food consumption) occurred, and fetal deaths, fetal cardiomegaly and fetal dilated aortae were observed at systemic exposure levels (AUC) 36-fold the MRHD.

In a pre- and postnatal developmental study, rats were treated with daily oral doses of mirabegron at 0, 10, 30, or 100 mg/kg/day (0, 1, 6, or 22-fold the MRHD) from day 7 of gestation until day 20 after birth. Decreased maternal body weight was observed along with decreased pup survival in the first few days after birth (92.7% survival) compared to the control group (98.8% survival), at 100 mg/kg/day (22-fold the MRHD). Pup body weight gain was reduced until postnatal day 7 but not further affected throughout the remainder of the lactation period. In utero and lactational exposure did not affect developmental milestones, behavior or fertility of offspring. No effects were observed at 30 mg/kg/day.

#### Lactation

##### Risk Summary

There is no information on the presence of mirabegron in human milk, the effects on the breastfed child, or the effects on milk production. Mirabegron-related material was present in rat milk and in the stomach of nursing pups following

administrations of a single 10 mg/kg oral dose of 14C-labeled mirabegron to lactating rats.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for MYRBETRIQ and any potential adverse effects on the breastfed child from MYRBETRIQ or from the underlying maternal condition.

#### **Pediatric Use**

The safety and effectiveness of MYRBETRIQ in pediatric patients have not been established.

#### **Geriatric Use**

No dose adjustment is necessary for the elderly. The pharmacokinetics of MYRBETRIQ is not significantly influenced by age. Of 5648 patients who received MYRBETRIQ in the phase 2 and 3 studies, 2029 (35.9%) were 65 years of age or older, and 557 (9.9%) were 75 years of age or older. No overall differences in safety or effectiveness were observed between patients younger than 65 years of age and those 65 years of age or older in these studies.

#### **Renal Impairment**

MYRBETRIQ has not been studied in patients with end stage renal disease ( $CL_{cr} < 15$  mL/min or  $eGFR < 15$  mL/min/1.73 m<sup>2</sup> or patients requiring hemodialysis), and, therefore is not recommended for use in these patient populations.

In patients with severe renal impairment ( $CL_{cr}$  15 to 29 mL/min or  $eGFR$  15 to 29 mL/min/1.73 m<sup>2</sup>), the daily dose of MYRBETRIQ should not exceed 25 mg. No dose adjustment is necessary in patients with mild or moderate renal impairment ( $CL_{cr}$  30 to 89 mL/min or  $eGFR$  30 to 89 mL/min/1.73 m<sup>2</sup>).

#### **Hepatic Impairment**

MYRBETRIQ has not been studied in patients with severe hepatic impairment (Child-Pugh Class C), and therefore is not recommended for use in this patient population.

In patients with moderate hepatic impairment (Child-Pugh Class B), the daily dose of MYRBETRIQ should not exceed 25 mg. No dose adjustment is necessary in patients with mild hepatic impairment (Child-Pugh Class A).

#### **Gender**

No dose adjustment is necessary based on gender. When corrected for differences in body weight, the MYRBETRIQ systemic exposure is 20% to 30% higher in females compared to males.

### -----OVERDOSAGE-----

Mirabegron has been administered to healthy volunteers at single doses up to 400 mg. At this dose, adverse events reported included palpitations (1 of 6 subjects) and increased pulse rate exceeding 100 bpm (3 of 6 subjects). Multiple doses of mirabegron up to 300 mg daily for 10 days showed increases in pulse rate and systolic blood pressure when administered to healthy volunteers. Treatment for overdosage should be symptomatic and supportive. In the event of overdosage, pulse rate, blood pressure and ECG monitoring is recommended.

### -----NONCLINICAL TOXICOLOGY-----

#### **Carcinogenesis, Mutagenesis, Impairment of Fertility**

##### **Carcinogenicity**

Long-term carcinogenicity studies were conducted in rats and mice dosed orally with mirabegron for two years. Male rats were dosed at 0, 12.5, 25, or 50 mg/kg/day and female rats and both sexes of mice were dosed at 0, 25, 50, or 100 mg/kg/day. Mirabegron showed no carcinogenic potential at systemic exposures (AUC) 38 to 45-fold higher in rats and 21 to 38-fold higher in mice than the human systemic exposure at the 50 mg dose.

##### **Mutagenesis**

Mirabegron was not mutagenic in the Ames bacterial reverse mutation assay, did not induce chromosomal aberrations in human peripheral blood lymphocytes at concentrations that were not cytotoxic, and was not clastogenic in the rat micronucleus assay.

##### **Impairment of Fertility**

Fertility studies in rats showed that mirabegron had no effect on either male or female fertility at non-lethal doses up to 100 mg/kg/day. Systemic exposures (AUC) at 100 mg/kg in female rats was estimated to be 22-fold the MRHD in women and 93-fold the MRHD in men.

### -----PATIENT COUNSELING INFORMATION-----

Advise the patient to read the FDA-approved patient labeling (Patient Information).

- Inform patients that MYRBETRIQ may increase blood pressure. Periodic blood pressure determinations are recommended, especially in patients with hypertension.
- Inform patients that MYRBETRIQ has also been associated with infrequent urinary tract infections, rapid heartbeat, rash, and pruritus.
- Inform patients that urinary retention has been reported when taking MYRBETRIQ in combination with muscarinic antagonist drugs used in the treatment of overactive bladder. Instruct patients to contact their physician if they experience these effects while taking MYRBETRIQ.
- Inform patients that MYRBETRIQ, when taken in combination with solifenacin succinate, has been associated with dry mouth, urinary tract infection, constipation, and tachycardia..

#### **Rx Only**

Marketed and Distributed by:  
**Astellas Pharma US, Inc.**  
Northbrook, Illinois 60062

MYRBETRIQ® is a registered trademark of Astellas Pharma Inc. All other trademarks or registered trademarks are the property of their respective owners.

© 2012 – 2018 Astellas Pharma US, Inc.

Revised: April 2018

206813-BRFS

057-3103-PM

## Botulinum Neurotoxin for Sexual Dysfunction

▼ Continued from page 13

the treatment group demonstrated a statistically significant increase in mean intravaginal ejaculatory latency time (2.35 minutes) compared to the control group (0.79 minutes) and baseline (0.74 minutes). Six patients had side effects from therapy, which included decreased erectile hardness in 4 and incomplete urination in 2. These changes resolved spontaneously without additional intervention.

Dyspareunia often originates from myofascial trigger points, which are small bands of muscle that produce sustained contraction when irritated, that form in the pelvic region. BoNT injections into the pelvic floor may alleviate dyspareunia by providing a direct analgesic effect, which prevents excessive muscle spasm associated with these myofascial trigger points. Few human studies have been reported in the literature but there are reports of decreased pain after treatment.<sup>1</sup>

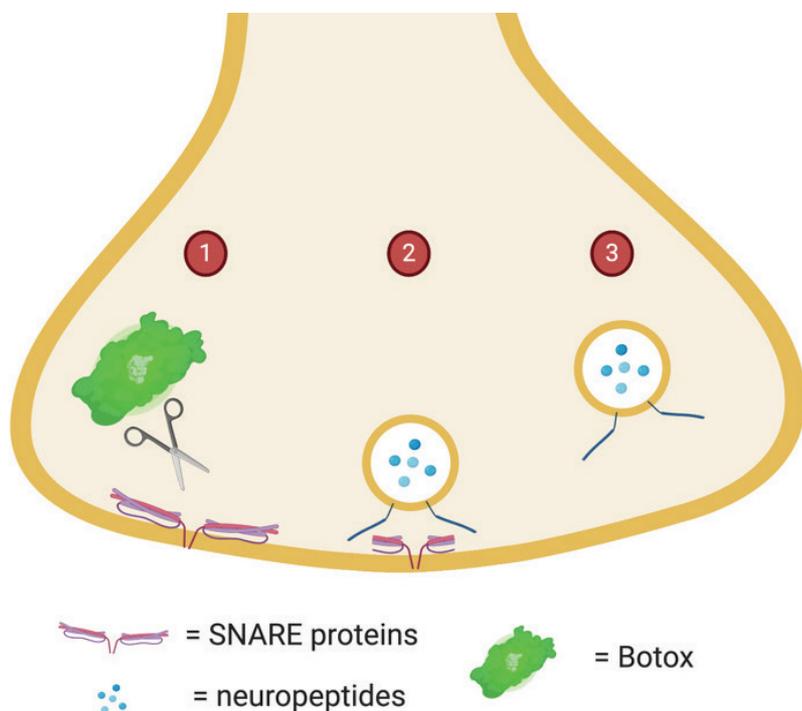
Vaginismus can be caused by a psychological (anxiety) and/or physical (muscle spasm, pain) disorder. Electromyography performed on women with vaginismus revealed that light touch or examination can cause abnormally high levels of muscle activity in the levator ani and bulbocavernosus muscles. BoNT injections help these patients by inhibiting ACh release at the neuromuscular junction, causing relaxation of the musculature. In the largest human study to date more than 200 women with refractory vaginismus received

BoNT injections into the bulbospongiosum.<sup>1</sup> At 5-week followup 71% were able to engage in pain-free intercourse.

Vestibulodynia can be provoked (insertion, contact) or spontaneous, and occurrence can be intermittent, persistent, constant, immediate or delayed. BoNT is suggested to reduce discomfort by decreasing peripheral release of SP, CGRP and other neuropeptides associated with pain. Decreased release of these neuropeptides resulted in reduced sensitization of peripheral nociceptive fibers, thereby reducing pain. In human studies BoNT injection into the bulbospongiosus muscles decreased patient reported pain for almost a full year after treatment.<sup>1</sup>

Persistent genital arousal disorder (PGAD) is a rare condition with recent research limited to case based analyses. There is no standard of care for patients with this condition, although selective serotonin reuptake inhibitors, dopamine agonists, anti-epileptics and cognitive behavioral therapy have all been tried with varying levels of success. BoNT is hypothesized to treat PGAD by inhibition of peripheral glutamate release, and decreased CGRP and SP release. Two patients with PGAD reported clinical improvement after treatment with periclitral BoNT injection.<sup>1</sup>

Sexual dysfunctions in men and women are distressing conditions that are often difficult to manage. BoNT is a rational and safe treatment option that can be considered in patients with refractory disease who have not responded to other therapies. ♦



**Figure 2.** Effect of botox on presynaptic neuron. 1, Botox cleaves SNARE proteins attached to presynaptic membrane. 2, Without SNARE proteins vesicle is unable to dock or fuse with presynaptic membrane. 3, Neuropeptides (ACh, SP, CGRP etc) remain in presynaptic neuron and are not released into synapse.

## Appendix 1. Hypothesized BoNT mechanism of action for treating sexual disorders.

Disorder	Mechanism
Chronic scrotal pain	Decreased release of SP and CGRP
Erectile dysfunction	Inhibition of neuropeptide release from adrenergic and cholinergic neurons in the corpora cavernosa
Premature ejaculation	Inhibition of ACh release at the neuromuscular junction of the bulbospongiosus muscles
Dyspareunia	Local anesthetic effect and inhibition of ACh release at the neuromuscular junction
Vaginismus	Inhibition of ACh release at the neuromuscular junction
Vestibulodynia	Decreased release of SP and CGRP
Persistent genital arousal disorder	Decreased release of glutamate, SP, CGR, and downregulation of transient receptor cation channel subfamily V member 1

## Appendix 2. Definitions of female sexual disorders.

Disorder	Definition
Dyspareunia	Genital pain associated with sexual intercourse
Vaginismus	The inability to tolerate vaginal penetration despite the desire to do so
Vestibulodynia	Vestibular pain without a clear identifiable cause that lasts at least 3 months
Persistent genital arousal disorder	Physiological symptoms of sexual arousal that are distressing or painful and are 1) unrelated to subjective sexual desire, 2) not triggered by sexual activity and 3) do not resolve with orgasm

- Dick B, Natale C, Reddy AG et al: Application of botulinum neurotoxin in female sexual and genitourinary dysfunction: a review of current practices. *Sex Med Rev* 2020; doi:10.1016/j.sxmr.2020.01.003.
- Calixte N, Brahmabhatt J and Parekattil S: Chronic testicular and groin pain: pathway to relief. *Curr Urol Rep* 2017; **18**: 83.
- Ghanem H, Raheem AA, AbdelRahman IFS et al: Botulinum neurotoxin and its potential role in the treatment of erectile dysfunction. *Sex Med Rev* 2018; **6**: 135.
- Li ZT, Li YF, Zhang Y et al: [Injection of botulinum-A toxin into bulbospongiosus muscle for primary premature ejaculation: a preliminary clinical study]. *Zhonghua Nan Ke Xue* 2018; **24**: 713.

**Urology Care**  
FOUNDATION™  
*The Official Foundation of the American Urological Association*

## Explore Our Free Patient Education Materials

**NEW! Select resources are now available in a variety of languages.**

- Prostate Health Playbook
- Spanish Men's Urology Health Poster
- Brazilian Portuguese Stress Urinary Incontinence Patient Guide
- Italian Erectile Dysfunction Patient Guide

**CLEAR, CREDIBLE AND COMPREHENSIVE**  
ORDER OR DOWNLOAD AT  
[UrologyHealth.org](http://UrologyHealth.org)

## RADIOLOGY Corner

## Small Renal Mass



Michael J. Biles, MD



Phillip Pierorazio, MD

Baltimore, Maryland

A healthy, 73-year-old woman presented to the urology clinic with an incidentally diagnosed small renal mass (SRM) at an outside hospital. Computerized tomography (CT) revealed a right 1.4 cm solid heterogeneous mass on the anterior midpole of the right kidney. She was counseled about treatment options including active surveillance (AS) or definitive therapy, and she elected to be enrolled in the Delayed Intervention and Surveillance for SRM (DISSRM) Registry.

Repeat CT at 6-month followup showed an increase in the size of the mass to 1.8 cm. In early 2015 the mass was 2.2 cm and by August it had grown to 2.7 cm. Given the persistent growth of the mass the patient was counseled on definitive treatment and elected to undergo partial nephrectomy. In lieu of biopsy, a sestamibi scan was performed, which indicated a likely malignancy. A robot-assisted laparoscopic partial nephrectomy was performed 2 years after initial diagnosis which revealed a 1 cm clear cell renal cell carcinoma (RCC) (stage cT1a, International Society of Urological Pathology grade II). The patient remains disease-free 5 years later.

RCC has undergone a stage migration in the United States in which 70% of newly detected renal tumors are localized and low stage (cT1a) due to earlier detection by increased use of imaging modalities.<sup>1</sup> The American Urological Association guidelines endorse AS or definitive treatment including surgery (partial nephrectomy preferred over radical nephrectomy) or ablative techniques such as cryosurgery or radio frequency ablation for the management of SRMs suspicious for cT1a RCC due to their equivalent oncologic outcomes.<sup>2,3</sup>

AS is a safe initial management

strategy and particularly recommended for patients with a renal mass smaller than 2 cm, decreased life expectancy or multiple medical comorbidities. AS protocols can vary but consist of serial imaging. The DISSRM Registry, which includes patients from Johns Hopkins, Columbia University and Beth Israel Deaconess, opened in 2009 and currently follows more than 500 patients under AS with serial imaging every 6 months for the first 2 years and annually thereafter.

Criteria determining which patients on AS should cross over to undergo delayed intervention (DI)

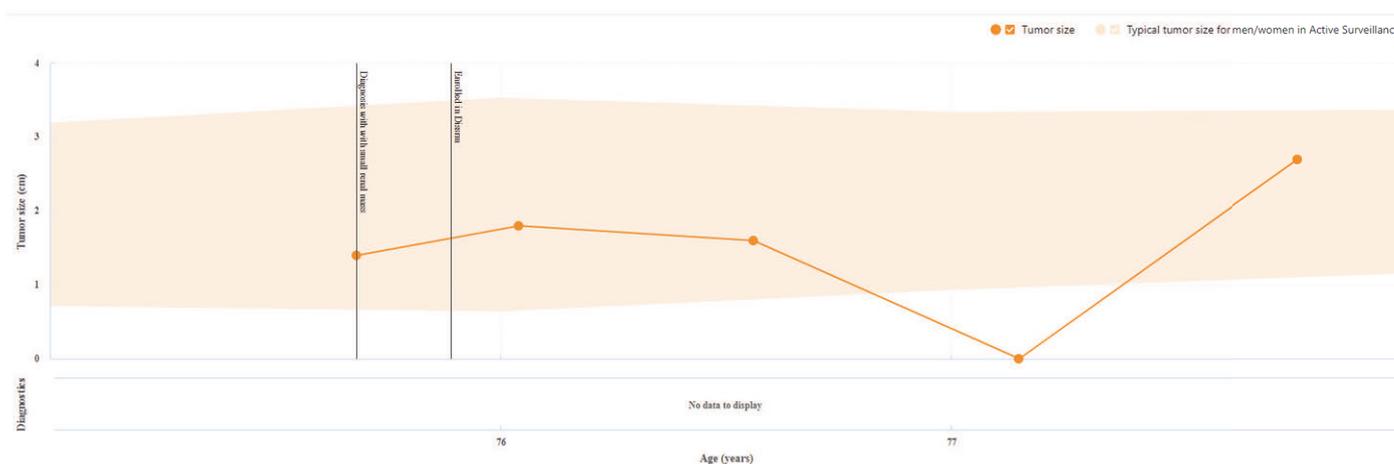
are elevated tumor growth rates greater than 0.5 cm per year, tumor diameter progression to greater than 4 cm (cT1b) or patient preference. However, growing data challenge the initial recommendations for DI. A recent review of the DISSRM registry revealed that 12.4% of patients on AS pursued DI at a median of 12 months. About half the patients underwent DI for tumor growth rates greater than 0.5 cm per year and half based on patient preference or anxiety.

Interestingly, only 19% of patients undergoing surgery had unfavorable pathology (pT3 or high grade), and growth rate greater than 0.5 cm per year did not impact the rate of RCC, high grade disease or pathological up staging, suggesting growth rate is not a strong predictor of adverse pathology for patients with cT1a RCC (fig. 1).<sup>4</sup> However, tumor size is predictive of

tumor grade, up-staging at the time of surgery and crossover from AS to DI.<sup>5</sup> Metadata indicate that the likelihood of low risk RCC (cT1a and grade 2 or lower) for tumors smaller than 2 cm, 2 to 3 cm, 3 to 4 cm, 4 to 6 cm and more than 6 cm are 89%, 85%, 77%, 66% and 50%, respectively. These findings affirm that tumor size is a greater predictor of biology than growth rate.<sup>6</sup>

Active surveillance for small renal masses reflects known data regarding indolent tumor biology and reduces unnecessary procedures. A better understanding of tumor progression and refinement of criteria for delayed intervention will improve patient selection for crossover, thereby further reducing unnecessary procedures in patients who harbor low risk disease and better identify those with higher risk disease (fig. 2). ♦

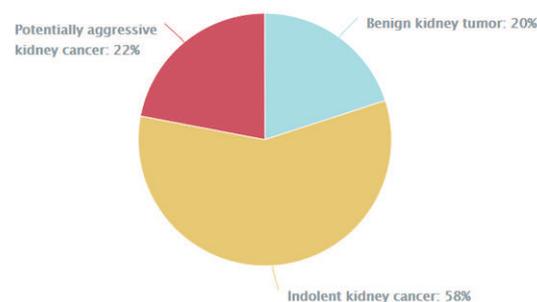
Tumor size



**Figure 1.** Tumor growth curve generated from Active Care–DISSRM application displaying size of tumor while patient was on AS. Tumor was not visualized on surveillance ultrasound, hence value of 0 for that time point. Tumor increased by approximately 1 cm within 1 year.

A

If patients with similar diagnosis, and kidney tumor size had surgery today, what is the likelihood of you having a benign tumor(s), having indolent (non-aggressive) cancer, dying of kidney cancer, or dying of other causes?



B

If 100 people like you enrolled in Active Surveillance after 5 years...



**Figure 2.** Predicted kidney cancer outcomes. Charts from Active Care–DISSRM application predicting oncologic outcomes based on individual tumor characteristics. A, patient risk of harboring benign disease, indolent or potentially aggressive (high grade or stage 3) renal cell carcinoma, based on patients who underwent immediate surgery in the DISSRM Registry. B, likelihood of possible outcomes for patient if enrolled in AS protocol for 5 years, including remaining on AS, undergoing treatment for kidney tumor, dying of unrelated causes or dying of kidney cancer. These figures provide an important visualization based on patient's individual and tumor characteristics to help counsel on and choose specific treatment options.

1. Patel HD, Gupta M, Joice GA et al: Clinical stage migration and survival for renal cell carcinoma in the United States. *Eur Urol Oncol* 2019; **2**: 343.
2. Campbell S, Uzzo RG, Allaf ME et al: Renal mass and localized renal cancer: AUA guideline. *J Urol* 2017; **198**: 520.
3. Alam R, Patel HD, Osumah T et al: Compar-

ative effectiveness of management options for patients with small renal masses: a prospective cohort study. *BJU Int* 2019; **123**: 42.

4. Gupta M, Alam R, Patel HD et al: Use of delayed intervention for small renal masses initially managed with active surveillance. *Urol Oncol* 2019; **37**: 18.
5. McIntosh AG, Ristau BT, Ruth K et al: Active

surveillance for localized renal masses: tumor growth, delayed intervention rates, and >5-yr clinical outcomes. *Eur Urol* 2018; **74**: 157.

6. Patel HD, Semerjian A, Gupta M et al: Surgical removal of renal tumors with low metastatic potential based on clinical radiographic size: a systematic review of the literature. *Urol Oncol* 2019; **37**: 519.

# Approach to Dietary Induced Hyperoxaluria: Why the Low Oxalate Diet Does Not Work



**Kristina L. Penniston, PhD, RDN, FAND**  
Madison, Wisconsin

In 20 years as the registered dietitian nutritionist for our multidisciplinary metabolic stone clinic I have seen many patients on a low oxalate diet (LOD). Some bring the handout they were given along their stone journey providing the usual list of purportedly high oxalate foods, a list that differs dramatically among sources. Others typed the words “kidney stone” into their web browser and then followed links to details about oxalate. After a while I started asking, “Why are these patients still forming stones?”

Granted, it is possible that patients whose stone recurrence is stymied on a LOD are not currently seeking prevention. However, even if true, why do so many others experience relapse? One reason is simply that patients whose stone composition is not primarily calcium oxalate (CaOx) will continue to form stones on a LOD.

This may seem like a no-brainer, but I see many patients who were told by a provider to limit oxalate even though the stones were primarily or totally uric acid, struvite or even cystine. In these cases a low oxalate prescription is akin to prescribing blood pressure medication to a patient without high blood pressure. Even in patients forming primarily CaOx stones, without identifying hyperoxaluria initiating a LOD is like starting an antibiotic without knowing which microbe you are treating.

When first asked to write this article, the proverbial can of worms came to mind. After all, dispensing with the idea that a LOD is therapeutic against all types of stones, this diet for preventing CaOx stones is still dogma that has been promoted for decades and longer. It is in the AUA guidelines for medical management of stones<sup>1</sup> and pervades the internet (resulting in a “tangled web”<sup>2</sup> of information). The LOD is a therapeutic diet option in hospitals, emergency room handouts given to patients with acute stones recommend it<sup>3</sup> and it is often the piece of preventive advice (or one of

only a few) that patients ever receive. Notwithstanding the unleashed worms, I question this dogma. 1) Is a LOD essential for reducing hyperoxaluria? 2) Is there sufficient evidence for a LOD to prevent CaOx stones? 3) What is a LOD? Is it the same for everyone? 4) Are there unwanted side effects? 5) Are there ever indications for a LOD?

First, hyperoxaluria is multifactorial, and individual factors sometimes converge. There is debate about whether to consider urinary oxalate (UOx) as a dichotomous risk (typically greater than 40–45 mg per day) or as a continuous variable to be minimized as much as possible.<sup>4</sup> Potential contributors to high UOx and corrective actions are described in the Appendix. Effective strategies to treat hyperoxaluria do not include reducing oxalate intake if there is some other cause.

Second, there is less evidence for a LOD than many may realize and arguably more for reducing the potential bioavailability of oxalate (PBO) in the diet. During much of human evolution oxalate intake was likely quite high from the foraging of leafy greens, grasses, nuts, seeds, roots and tubers. Interestingly and perhaps not coincidentally, these same foods were rich in calcium. As Heaney points out, “the annual rack of antlers produced by deer in northern latitudes is testimony to the environmental abundance of calcium” from these same foods.<sup>5</sup>

Unfortunately, the abundance of commonly consumed plant cultivars rich in oxalate and calcium has been significantly reduced over millennia. For this and other reasons, the calcium intake of most Americans who do not supplement is less than the recommended 1,000 mg per day for most adults. Normalizing calcium intake (or increasing it to match higher oxalate intake) and timing it with meals is a legitimate first line alternative to a LOD.

Third, there is no uniform definition of a LOD. Recommendations for less than 100 or even 50 mg per day are typical, but where do these numbers originate? If PBO is adequately controlled, does it matter how much is consumed? Moreover, because of highly variable and sometimes

obviously erroneous reports of food oxalate, does anyone really know how much oxalate they eat? I see many patients whose oxalate intakes are extremely high but whose UOx excretion is controlled. The converse is also true. Given the multiplicity of factors contributing to hyperoxaluria (Appendix), not to mention variability in the way individuals digest and absorb foods, there is unlikely ever to be a uniform LOD for all.

Fourth, “What’s the harm of dietary recommendations?” Dietitians hear this a lot, especially from non-dietitians. While nutrition interventions may seem harmless, this is not always true. As with any medical therapy there are consequences when inappropriately prescribed. A LOD is a restricted diet. Because oxalate is fairly widely distributed in the food supply, foods from many categories are implicated. There are several potential nutritional consequences.

- Nutrition quality is lower. Restricted foods may be unique sources of nutrients and other healthy food-derived components, including CaOx

stone inhibitors (eg bicarbonate precursors, magnesium, phytate, fiber, prebiotics) and CaOx stone risk has been shown to increase on a LOD.<sup>6</sup>

- A LOD may restrict foods recommended for managing other comorbidities.
- A healthy gut microbiome is diverse, and microbial diversity requires a breadth of substrate, including oxalate. Consequences of a long-term LOD beyond reducing oxalate degradation capacity are not known.
- Lowering dietary oxalate does not address other reasons CaOx stones form, resulting in unnecessary and meaningless therapy and violation of the edict to “first do no harm.”
- A misappropriated LOD, ie when it does not address the true etiology of high UOx, fails to reduce stone risk/formation, and risks lost faith in nutrition therapy and enthusiasm for

▼ Continued on page 22

**Table.** Foods commonly used in juicing and their reported oxalate content listed with oxalate content per household measure.<sup>7</sup>

	Food, Quantity	Oxalate (mg)
Relatively higher oxalate content	Raw spinach, 1 cup <sup>a</sup>	656
	Beets, ½ cup <sup>a,b</sup>	76
	Okra, ½ cup <sup>a,b</sup>	57
	Raspberries, 1 cup	48
	Orange, 1 fruit	29
	Avocado, 1 fruit	19
	Tahini, 1 tbsp	16
	Peanut butter, 1 tbsp	13
	Raw carrots, ½ of a “large” carrot	10
	Collards, 1 cup <sup>a,b</sup>	10
Low oxalate content often mistaken for high	Blueberries, 1 cup	4
	Pineapple, 1 cup <sup>a</sup>	4
	Mustard greens, 1 cup chopped <sup>b</sup>	4
	Banana, 1 fruit	3
	Raw celery, 1 stalk	3
	Raw kale, 1 cup chopped	2
	Applesauce, 1 cup	2
	Blackberries, ½ cup	2
	Strawberries, ½ cup <sup>a</sup>	2
	Apple, 1 fruit	1
	Broccoli, ½ cup chopped <sup>b</sup>	1
	Cabbage, ½ cup <sup>a,b</sup>	1
	Cucumber, ¼ of a cucumber <sup>a,b</sup>	1
	Endive, ½ cup <sup>a</sup>	0
	Iceberg lettuce, 1 cup <sup>a,b</sup>	0
	Romaine lettuce, 1 cup <sup>a,b</sup>	0

<sup>a</sup> Not specified if whole, chopped or otherwise adulterated

<sup>b</sup> Not specified if raw or cooked

## Dietary Induced Hyperoxaluria

▼ Continued from page 21

### prevention

Fifth, I won't say I never advise lower oxalate intake. Patients for whom I might recommend a lower oxalate intake include those whose higher UOx I suspect to be from juicing. Some commonly used foods are high in oxalate (see table). However, in my practice I typically advise to add calcium fortified nondairy milk, yogurt, kefir or dairy milk to the blender in an effort to lower the PBO of the juice, to lower the quantity of high oxalate foods and/or to substitute lower oxalate foods as needed. Patients whose oxalate intake may require significant restriction are those whose high UOx is unresponsive to other strategies such as severe malabsorption for which calcium intake cannot be increased further. ♦

1. Pearle MS, Goldfarb DS, Assimos DG et al: Medical management of kidney stones: AUA guideline. *J Urol* 2014; **192**: 316.
2. Attalla K, De S and Monga M: Oxalate content of foods: a tangled web. *Urology* 2014; **84**: 555.
3. Sternberg KM, Pham A, Cisu T et al: Discharge materials provided to patients with kidney stones in the emergency department may be a source of misinformation. *Can J Urol* 2018; **25**: 9585.
4. Prochaska M, Taylor E, Ferraro PM et al: Relative supersaturation of 24-hour urine and likelihood of kidney stones. *J Urol* 2018; **199**:

**Appendix.** Factors causing or contributing to hyperoxaluria (defined variably as less than 40 or 45 mg in 24-hour urine collection). Specific contributors to higher urinary oxalate excretion are listed along with proposed mechanisms of action and corrective strategies.

General Factors	Specific Contributors	Mechanisms of Action	Corrective Strategies
Oxalate related dysbiosis	Suboptimal oxalate-degrading capacity of gut microbiome	Insufficient dietary substrate to colonize and support proliferation of oxalate-degrading microbes	Increase and optimize intake of a variety of fiber-rich foods
		Antibiotics or other external agent/medication that deplete gut microbes	Minimize exposure if possible; consume fiber-rich diet; probiotic supplementation may help but evidence limited
High PBO in diet	Insufficient intake of oxalate absorption inhibitors	Suboptimal intake of calcium and (to lesser extent) magnesium in context of usual oxalate intake and especially in context of malabsorption from short bowel, gastric bypass, inflammatory bowel etc	Increase intake of calcium (and to extent possible, magnesium) relative to oxalate intake; pair with meals to reduce PBO
		Excessive intake of promoters of oxalate absorption	Increase intake of inhibitors (as above)
	Excessive biosynthesis of oxalate	Deficient or absent enzyme activity or other metabolic disorder	Other than inborn error of metabolism (as in the Primary Hyperoxalurias, PH), vitamin B6 deficiency could promote excessive biosynthesis
	Excessive supplementation of oxalate precursors or those with high oxalate loads	Vitamin C supplements (degraded to oxalate; amount triggering response varies between individuals)	Eliminate supplements
		Excessive intake or supplements of oxalate precursors (collagen, hydroxyproline) Supplements high in oxalate (eg cinnamon, turmeric, alfalfa, potentially other plant-derived concentrates)	↓

1262.

5. Heaney RP: The roles of calcium and vitamin D in skeletal health: an evolutionary perspective. *J Food Nutr Agric* 1997; **20**: 4.
6. Noori N, Honarkar E, Goldfarb DS et al: Uri-

nary lithogenic risk profile in recurrent stone formers with hyperoxaluria: a randomized controlled trial comparing DASH (dietary approaches to stop hypertension)-style and low-oxalate diets. *Am J Kidney Dis* 2014; **63**: 456.

7. Harvard T.H. Chan School of Public Health: Directory listing of /health/Oxalate/files. Harvard University 2017. Available at <https://regepi.bwh.harvard.edu/health/Oxalate/files>. Accessed March 16, 2020.

## PRACTICE Tips & Tricks

# Urologists Moving from Triple to Quadruple Aim



**Neil H. Baum, MD**  
New Orleans, Louisiana

More urologists are experiencing dissatisfaction with their practices, which is an early warning sign of burnout. A common complaint from our colleagues is that we are spending an inordinate amount of time on computers and less time on patient care. It is also of interest that our patients are complaining that physicians are looking more at the computer and entering data than focusing on them.

The Triple Aim has lofty goals of improving outcomes, reducing costs

and increasing patient satisfaction, but it cannot be achieved unless we add the fourth component of physician satisfaction. We should consider calling on our leadership at the AUA, our sections and—yes—even the American Medical Association to help us reach the Fourth Aim.

### A Few Suggestions to Move from Triple to Quadruple Aim

Reduce the time physicians spend on the computer entering patient data.

Make more use of nurses, medical assistants or other staff who can enter some or all documentation into the electronic health record, assisting with order entry, prescription writing and charge capture. These are

activities that don't require 8 to 10 years of medical training to accomplish. Urologists should do what we do best, which is diagnose and treat urological conditions, rather than enter data into a computer.

Use pre-visit planning and pre-appointment laboratory testing to reduce time wasted on the review and followup of laboratory results. For example, if a man comes for his annual exam, request the prostate specific antigen test before the visit and have the results of the test available prior to the office visit. Now the patient has only 1 visit and no followup or phone calls are required. This measure will open more slots in our schedule for new patients or patients requiring more time.

Ask our leaders and specialty organizations to create useful and practical guidelines to legally expand roles allowing nurse practitioners,

physician assistants and medical assistants to assume responsibility for urological care under supervision.

Embrace new technology such as telemedicine. An AUA census conducted in 2018 revealed a trend of more urban medical practices embracing telemedicine. From 2011 to 2016 telehealth service use nationally increased substantially, especially in rural areas (960%) compared to urban areas (629%). Using telemedicine will certainly increase the efficiency and productivity of the practice. Legal caveats must be made clear on a state by state basis so that doctors can safely and securely make use of telemedicine without going afoul of the law.

To avoid shifting burnout from physicians to practice staff, ensure that staff who assume responsibilities

▼ Continued on page 23

HAVE YOU *Read?*

**Daniel Shoskes, MD**  
Cleveland, Ohio

**Grashow R, Weisskopf MG, Miller KK et al: Association of concussion symptoms with testosterone levels and erectile dysfunction in former professional US-style football players. JAMA Neurol 2019; 76: 1428–1438.**

Head trauma in football players can lead to significant neurological problems later in life. Can it also impact sexual function? Grashow et al explore the associations between concussion symptom history and participant reported indicators of low testosterone levels and erectile dysfunction (ED). This cross sectional study of former professional U.S.-style football players was conducted using surveys on past football exposures, demographic factors and current health conditions.

Of the 13,720 male former players eligible to enroll who were contacted 3,506 (25.6%) responded. In 3,409 former players (mean age 52.5 years, SD 14.1) the prevalence of indicators of low testosterone levels and ED were 18.3% and 22.7%, respectively. The odds of reporting low testosterone levels or ED indicators were elevated for previously established risk factors (eg diabetes, sleep apnea and mood disorders). Models adjusted for demographic characteristics, football exposures and current health factors showed a significant increasing association

of concussion symptom score with the odds of reporting the low testosterone indicator (highest vs lowest quartile, OR 2.39, 95% CI 1.79–3.19,  $p < 0.001$ ). The ED indicator had a similar association (highest quartile vs lowest, OR 1.72, 95% CI 1.30–2.27,  $p < 0.001$ ).

The authors conclude that concussion symptoms at the time of injury among former football players are associated with current participant reported low testosterone levels and ED indicators. These findings suggest that men with a history of head injury may benefit from discussions with their health care providers regarding testosterone deficiency and sexual dysfunction.

**Wills BW, Smith WR, Arguello AM et al: Association of surgical jacket and bouffant use with surgical site infection risk. JAMA Surg 2020; doi:10.1001/jamasurg.2019.6044.**

And so the bouffant cap raises its billowy head again but now with the added fashion statement of forearm covering surgical jackets, representing another in a line of evidence-free mandates to improve perceived patient safety. Wills et al evaluate whether the combination of mandated surgical jackets and bouffants in the operating room is associated with the risk of surgical site infection. They performed a retrospective cohort study of 34,042 inpatient surgical encounters at a large academic tertiary care hospital during 3 periods corresponding with

implementation of surgical jackets and the subsequent mandate of surgical jackets plus bouffant head covers.

All inpatient surgical cases were included from the University of Alabama at Birmingham University Hospital, a single center, large academic tertiary care hospital. The temporal groups were no surgical jackets or bouffants mandated (8 months) vs surgical jackets mandated (6 months) vs surgical jackets and bouffants mandated (8 months). Of the total patients 16,380 were women (48%). There was no significant difference in the risk of surgical site infection (SSI) (1.01% vs 0.99% vs 0.83%,  $p=0.28$ ), mortality (1.83% vs 2.05% vs 1.92%,  $p=0.54$ ), post-operative sepsis (6.60% vs 6.24% vs 6.54%,  $p=0.54$ ) or wound dehiscence (1.07% vs 0.84% vs 1.06%, respectively,  $p=0.20$ ) among the 3 groups.

Receipts from the first 6 months of the 2018/2019 fiscal year provided an estimated expenditure of more than \$300,000 annually on surgical jackets. Bouffants were less expensive than surgical skull caps. The authors conclude that that surgical jackets and bouffants are neither beneficial nor cost-effective in preventing SSIs. Institutions should evaluate their own data to determine whether recommendations by outside governing organizations are beneficial and cost-effective.

**Zhou CK, Advani S, Chaloux M et al: Trends and patterns of testosterone therapy among US male medicare beneficiaries, 1999–2014. J Urol 2020; doi 10.1097/JU.0000000000000744.**

Testosterone normalization therapy can be highly effective for symptom improvement and comorbid disease modification but it is often prescribed capriciously without attention to appropriate diagnosis or monitoring. Zhou et al explored the Medicare database (1999 through 2014) to provide a comprehensive assessment of testosterone therapy (TT) patterns in the older U.S. male population. There were 392,698 incidents of patients using TT during 88 million person-years. Individuals using TT were predominantly younger, white nonHispanic and located in the South and West U.S. Census regions.

On average, TT dramatically increased during 2007 to 2014 (15.5% average annual change) despite a decrease in 2014. In 2014 the most commonly recorded potential indications for any TT use were hypogonadism (48%), fatigue (18%), erectile dysfunction (15%), depression (4%) and psychosexual dysfunction (1%). Laboratory tests to measure circulating testosterone concentrations for TT were infrequent with 35% having had at least 1 testosterone test in the 120 days before therapy, 4% had the recommended 2 pretests and 16% had at least 1 pretest and 1 posttest.

I am not concerned about the diagnosis codes, as we know how randomly unreliable they can be. It is depressing to see how little biochemical testing is performed to ensure the correct diagnosis and that the prescribed therapy is normalizing testosterone appropriately. We have to do better. ♦

## Practice Tips &amp; Tricks

▼ Continued from page 22

for patient care are well trained and understand that they are contributing to the health of their patients, and that unnecessary work is re-engineered out of the practice.

Our leadership needs to have a public relations campaign to address the chasm between society's expectations and the shrinking number of urologists, especially in rural areas.

Finally, more financial and personnel resources should be dedicated

to improving urologist satisfaction.

## The Bottom Line

I've heard many times that a successful marriage requires a happy spouse. If the spouse isn't happy, no one's happy. The same can be said for physician satisfaction. If the doctor isn't happy, no one—not staff or, more importantly, the patients—are going to be happy.

Let's direct our attention to making the urologist happy, and those other lofty Triple Aim goals will be achievable. ♦



**AUA MEMBERSHIP**  
*THERE'S VALUE IN BELONGING*

**EXPLORE YOUR BENEFITS!**

[www.AUAnet.org/Value](http://www.AUAnet.org/Value)

FROM THE *Chief Executive Officer*

## AUA Releases New Census Report, Launches 2020 Survey



**Michael T. Sheppard,**  
CPA, CAE  
Linthicum, Maryland

We recognize that all our members are being impacted by COVID-19, and

the AUA has taken great steps to support our community by canceling and postponing AUA activities and providing a Coronavirus Disease Information Center on our website. We also believe it is important to continue to communicate AUA's programs with our members and the broader urology community so they can access the information at their convenience.

The 2019 Census report helps to shed light on the urology workforce in the United States, and shows that we remain a dynamic, well-trained and hard-working specialty. In a 5-year (2015 vs 2019) comparison of Census reports the following key findings are noteworthy.

*Increase in number of actively practicing urologists.* In 2015, 11,990

urologists were identified as actively practicing in the United States. In 2019 the number of actively practicing urologists in the U.S. was 13,044, representing a 9.6% increase in this category.

*Growing number of female urologists.* The percentage of female practicing urologists increased to 9.9%, up from 7.7% in 2015. A higher proportion of female urologists was seen in the younger age group as more women are entering into and completing urology residency training.

*Increased fellowship training.* Approximately 40% of urologists have completed at least 1 fellowship program, up from 35.9% in 2015. The top areas of fellowship include oncology, endourology/stone disease and pediatrics.

*Practice settings.* Use of advanced practice providers (APPs) is evolving: approximately 53% of practicing urologists are in private practice, a decrease of more than 2% per year since 2015. The percentage

of employed urologists continued to increase from 51.3% in 2015 to 59.8% in 2019. Female urologists and urologists younger than 45 years are more likely to have employed status. The use of APPs is also growing as the percentage of urologists who work in their primary practice with at least 1 APP increased significantly from 62.7% in 2015 to 71.4% in 2019. Urologists working in academic medical centers are most likely to work with APPs.

*Use of telemedicine is growing.* In 2019 nearly 12% of U.S. urologists reported being compensated for using telemedicine, up from 8.8% in 2016 when the question was first asked in the Census. Urologists in metropolitan areas were more likely to use telemedicine than their counterparts outside metropolitan areas.

The 2019 Census also explored the subject of drug availability and pricing.

- 85% of urologists had patients who stopped taking their medications in the middle of established, successful

treatments because of a denial resulting from an insurance policy change. This occurred more often in non-metropolitan areas and in the south central United States.

- 90% of urologists had patients who stopped taking their medications because of an inability to afford them.
- More than half of urology practices in the United States accept drug samples from pharmaceutical companies for distribution to patients.

Each year the findings from the AUA Census play an important role in generating knowledge to inform urological care and workforce policy. The Census is a primary data source to explore the profession of urology, and I'd like to thank all of the members who took the time to be involved.

Please be a part of our 2020 report. Our newest Census survey is now available and members are urged to get involved by visiting [www.AUAnet.org/TakeCensus](http://www.AUAnet.org/TakeCensus). ♦

## AUA RESIDENTS & FELLOWS *Committee News*

### Control What You Can



**Joshua Belle, MBChB**  
South Central Section  
Representative, AUA  
Residents & Fellows  
Committee  
Omaha, Nebraska

Nearing the end of residency, I find myself reflecting on the last 5 years and the advice I would give myself if I began again. I have had a typical experience, from excited and terrified intern to overconfident senior and back again to excited and terrified chief, with many lessons along the way. I've felt the joy of successfully diagnosing and managing a complex case, the frustration of losing a battle against a disease, the burnout associated with electronic medical records and maintaining work-life balance, and the thrill of completing a case skin to skin for

the first time. I remember moments when I couldn't handle another page and moments when I couldn't wait to be in the operating room seeing a new technique.

I cannot offer much advice on the latter. After all, the pride and passion we enjoy when things go right is the reason we are in this profession. When we cut out a cancer, relieve the pain of a stone or improve quality of life, we all feel accomplished and fulfilled. It is the former where the advice is appreciated, on the days when we feel the true weight of our responsibility, our happiness is tenuous and our practice of medicine is a long way from perfect.

This cycle is recurring. It can be caused by an unpredictable postoperative complication, a nonadherent patient or something as simple as an instrument being unavailable or a

case being delayed. This advice is for those moments. You have likely heard some form of it before from Greek philosophy, an internet therapist or your mother. "It is not your fault, but it is your responsibility."<sup>1</sup>

I interpret this advice as "control what you can control." There are situations when we all react with frustration, annoyance, anger and even the rare internal monologue about how cosmically unfair something is. I now try to realize how unproductive this reaction is, how it removes the joy from my work and how it doesn't help me solve a problem, learn something new or grow in my career.

Because of this approach, I can orient myself appropriately as I move forward. I can choose to focus on what I can control and understand that reacting negatively to things I am powerless against does not benefit me or my patients. When I have time, I

can use it for preparation of what I can influence, and when I reflect I can spotlight the victories instead of the frustrations. I can try to take adverse circumstances as opportunities for positive social leadership instead of fostering a negative experience for the health care team. These are not skills I have perfected and, in fact, I struggle more often than not. However, when I look back at the end of my career I hope I can say I took my own advice.

I would like to thank my wife Erika, my father Ralph, astronaut Chris Hadfield and Mark Manson for all the advice mentioned in this article that I should have listened to long before I did. ♦

1. Manson M: The Subtle Art of Not Giving a F\*ck: A Counterintuitive Approach to Living a Good Life. San Francisco, California: HarperOne Publishing 2016.

FROM THE *Urology Care Foundation*

# Advancing Awareness of Women's Urological Health Resources and Initiatives during Women's Health Month



**Harris M. Nagler, MD, FACS**  
President, Urology Care Foundation  
New York, New York

As the world's leading urological health foundation, the Urology Care Foundation is proud of its commitment to advancing patient care through research and education. May is Women's Health Month and represents a fitting time to acknowledge the outstanding achievements women have made to urology and urological research.

For more than 40 years the Urology Care Foundation has fostered the development of women researchers and physician scientists while supporting their impactful journeys in this field. Through the Foundation's portfolio of research training awards, these outstanding individuals have emerged as research leaders who have catalyzed the advancement of urology practice while reducing the burden of disease on our patients.

Dr. Marguerite C. Lippert became the first woman to receive research scholar funding from the Foundation. Since our initial support of Dr. Lippert's research, we have continued to make significant strides. The Foundation has awarded more than \$8 million to 48 women researchers in the last decade.

These investments from the Foundation have had a lasting impact to drive critical improvements in patient lives. The Foundation has funded several areas of urology research, many of which were led by gifted female researchers, including benign prostatic hyperplasia, bladder cancer, incontinence, kidney cancer, overactive bladder, prostate cancer and urinary tract infections.

Earlier this year, we recognized recipients of our Research Scholar Awards, which included women researcher awardees Drs. Chen Qian, Diya Binoy Joseph, Morgan E. Roberts and Renea Sturm.

## Trailblazing Women in Urology Research

Two more outstanding research leaders I am privileged to highlight during this celebration of women in urology research are Drs. Lysanne Campeau and Margaret Pearle.

In 2015 Dr. Campeau earned the honor as the first woman to accept the Astellas Rising Stars in Urology

Research Award. Her work includes exploring metabolic syndrome as a potential cause of overactive bladder in order to develop new treatments.

Dr. Pearle became the first woman to earn the prestigious Gold Cystoscope award in 2003 for her notable contributions to patient care in the area of stone disease. She now holds the Ralph C. Smith Distinguished Chair in Urologic Education at the University of Texas Southwestern Medical Center.

## Patient Education and Women's Urology

The Foundation continues to provide the most current urological health information to patients through its multitude of resources and public awareness campaigns based on AUA

clinical guidelines.

The Foundation's Patient Education Council and Committees (PECC) are comprised of 6 committees responsible for delivering on our patient education mission. As it stands today the PECC include 11 women volunteers.

Many of our key patient education resources address urological issues that greatly impact women, such as incontinence, stress urinary incontinence, overactive bladder and urinary tract infection. We honor the women in urology and are grateful for their commitment to advancing the care of patients and the science of our field.

To learn more about these informative resources from the Urology Care Foundation and to share them with your patients, please visit [www.UrologyHealth.org](http://www.UrologyHealth.org). ♦

# SETTING THE STANDARD FOR UROLOGY WORLDWIDE



MORE EDUCATION | MORE RESOURCES  
MORE CONNECTIONS | MORE SAVINGS



American Urological Association

Advancing Urology™

*AUANet.org/Value*

# AUA VIRTUAL EXPERIENCE

**Stream AUA LIVE!**

**June 27-28, 2020**

**A Two-Day Virtual Education  
Experience Including Some of  
the Best Science from AUA!**

The AUA will host two days of virtual educational programming, including keynote lectures, sessions on new clinical guidelines, semi-live surgeries, late-breaking science, industry updates and more!

**FREE for AUA Members!**

**Learn More at [AUAnet.org/AUALIVE](https://AUAnet.org/AUALIVE)**



American  
Urological  
Association

Education & Research, Inc.

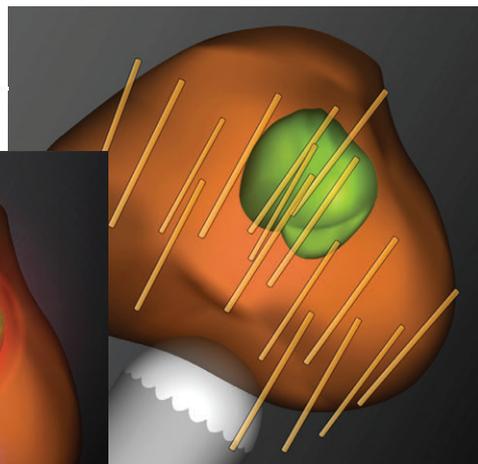
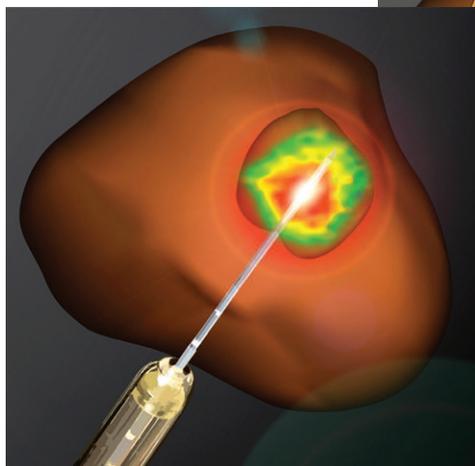


CLASSIFIED Ads

# Prostate Focal Therapy is Here. Are **You** Ready?

--- A **UCLA** fellowship can prepare you! ---

**Fusion Biopsy Experts.**



**Focal Therapy Innovators.**

Recent urology grads and current residents are invited to apply for a unique 1-year fellowship\*. At UCLA Urology, we train thought leaders in urologic oncology in a program emphasizing contemporary management of prostate cancer.

The UCLA opportunity provides a supportive, HIGH-VOLUME environment to learn **targeted prostate biopsy**, management of **active surveillance**, interpretation of **MRI**, and delivery of **focal therapies**---both approved (HIFU, Cryo) and under investigation (focal laser ablation).

*"My fellowship at UCLA has given me a career-launching experience with hundreds of targeted biopsies and focal therapy cases. I would do this again in a heartbeat."*

-Adam Kinnaird, MD PhD FRCSC, 2019-2020 Fellow

**Applications are now being accepted for July 2020**

Interested applicants should directly contact:  
**Dr. Leonard Marks at lmarks@mednet.ucla.edu**

Detailed description: <http://bit.ly/urologyFellowship2020>  
Youtube Channel: [targetedProstateBiopsy.com](http://targetedProstateBiopsy.com)

\*CA licensure/eligibility a pre-requisite.



## Urologist Cambridge Health Alliance (CHA)

Cambridge Health Alliance (CHA), is a nationally recognized, award-winning public healthcare system located in the Boston metro area. We are currently recruiting a Urologist to join our existing department (3 MDs & 1 PA). CHA is comprised of three hospital campuses and an integrated network of primary and specialty outpatient care sites.

CHA is an academic affiliate of Harvard Medical School (HMS) and Tufts University School of Medicine. Incoming MD will have opportunity to teach HMS Medical Students, HMS IM residents and Tufts FM residents.

- Academic appointment at HMS available commensurate with medical school criteria
- Call is 1:4. 24-hour consult triage, phone triage, and inpatient care is provided by in-house PA and surgical residents
- Fully integrated EMR (Epic)
- Research opportunities available
- Patient population provides unique opportunities if interested in health care disparities
- Salary commensurate with experience

CHA offers a collaborative practice environment and innovative clinical model. Candidates should possess excellent clinical and communication skills, and a commitment to our diverse, underserved patient population.

To confidentially apply visit [www.CHAproviders.org](http://www.CHAproviders.org) or email your CV/cover letter to Kasie Marchini at [ProviderRecruitment@challiance.org](mailto:ProviderRecruitment@challiance.org).

*We are an equal opportunity employer and all qualified applicants will receive consideration for employment without regard to race, color, religion, sex, sexual orientation, gender identity, national origin, disability status, protected veteran status, or any other characteristic protected by law.*

## AUANews Classified Advertising Information

Classified space is for advertising positions available, open faculty positions, course announcements, seminars, meetings and educational courses.

### Display Advertising Rates

Ad Size	1x	3x
Full Page	\$2,255	\$2,205
1/2 Page	\$1,850	\$1,770
1/4 Page	\$1,005	\$965
1/6 Page	\$720	\$710
Blind Box Services \$40 per issue		

### Line Advertising Rates

**\$260 for the first 50 words  
\$5.00 for every word thereafter**

### Closing Date & Cancellations:

Copy must be received six weeks in advance of the month in which the ad is to appear. Cancellation requests must be made in written form by fax, e-mail or postal mail and will be honored for the earliest applicable issue.

**ALL ADS  
MUST BE PREPAID**

### Contact:

Rhonda Truitt  
[rhonda.truitt@wt-group.com](mailto:rhonda.truitt@wt-group.com)  
P: 443-512-8899 x. 106 F: 443-490-4003

# USC Urology – Scientific Highlights

## Lancet Oncology

### Web Search Queries and Prostate Cancer: The Thin Line Between the Digital and Real World

Cacciamani G, Gill K, Gill IS. *Lancet Oncology* (April 2020)

We investigated the correlation between online Google searches-engine queries (SEQs) for PCa and metastatic PCa and its epidemiologic prevalence and variations according to U.S. Preventive Service Task Force (USPSTF) screening recommendations. SEQ trends correlate temporally and geographically with annual incidence of PCa, mPCa and PCa-mortality. This correlation increased further since the USPSTF recommendations (Fig.1a). U.S. state-by-state differences in SEQs reflect PCa-specific mortality in those states (Fig.1b). **Conclusion:** SEQs are a valid PCa-related public information resource and might serve as a complementary epidemiological tool. Providing accurate PCa-specific online information can deliver a valuable population-level service for patients and those related to them.

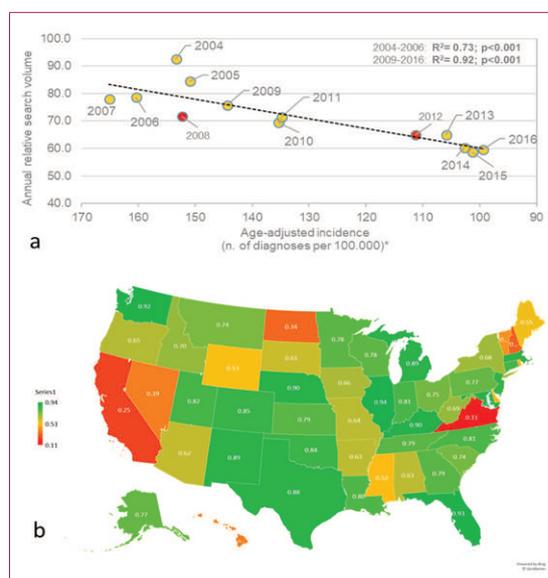


Fig 1 (a). Linear correlation between annual relative search volume (ARSV) and age-adjusted PCa incidence in the U.S.; two red dots reflect the 2008 and 2012 USPSTF recommendations.

Fig 1 (b) Heat-map chart showing U.S. state-by-state correlation between Google ARSV and age-adjusted PCa incidence (2009-2016). Epidemiological data from CDC, NPCR and NCI-SEER.

## Andrologia

### Opioid Prescription Patterns and Opioid Usage after Vasectomy

Asanad K, Nusbaum D, Samplaski M. *Andrologia*, in press 2020.

We determined urologists' opioid prescribing (e-survey) and patients' post-vasectomy pain control regimens (telephone survey). 52% of urologists routinely prescribed opioids post-vasectomy; yet, 42% of men did not actually use them. Of men using opioids, 53% used ibuprofen as their primary pain med vs 93% of men not using opioids ( $p=0.004$ ). Ibuprofen use correlated with using fewer opioid tablets ( $p=0.003$ ). **Conclusion:** Opioid prescription after vasectomy is common, yet not routinely necessary. Patients using ibuprofen used less opioids.

## British J. Urol. International

### Deep Learning on Automated Performance Metrics (APMs) and Clinical Features to Predict Urinary Continence Recovery after Robot-assisted Radical Prostatectomy (RRP)

Hung AJ, Chen J, Ghodoussipour S, Oh P, Liu Z, Nguyen J, Purushotham S, Gill I, Liu Y. *BJU Int.* 2019;124: 487

We predicted continence recovery in 100 RRP using a trained deep learning (DL) model (DeepSurv). For 8 surgeons, robotic APMs were captured prospectively and compared to their historical RRP (01/2015-08/2016). DeepSurv model features, ranked per importance in prediction, selected the top 4 surgeons "Group 1/APMs" versus others "Group 2/APMs". Continence rate: 79% @ 3 mos. Continence prediction by the DL model: CI 0.6; MAE 85.9. This model ranked APMs higher than patient features. In the historical cohort, "Group 1/APM" patients had superior continence @ 3 mos ( $p=0.034$ ) and 6 mos ( $p=0.047$ ). **Conclusions:** Using APMs and patient data, the DeepSurv model was able to predict continence after RRP. Surgeons with more efficient APMs had higher continence rates.

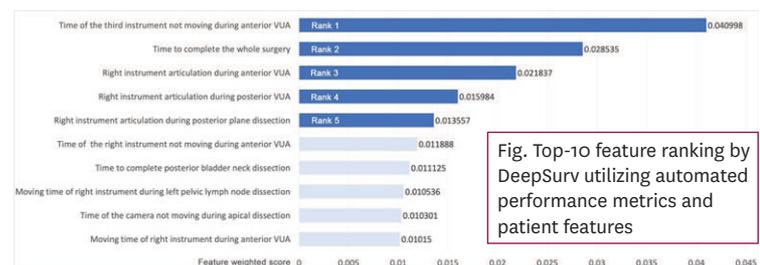


Fig. Top-10 feature ranking by DeepSurv utilizing automated performance metrics and patient features

## Physiology & Behavior

### Exercise Modulates Neuronal Activation in The Micturition Circuit: The MAPP Research Network Study

Daniel T, Holschneider P, Wang Z, Guo Y, Sanford M, Yeh J, Mao J, Zhang R, Rodriguez L. *Physiology & Behavior* 2020; 215, 112796

Stress exacerbates and exercise may improve symptoms of interstitial cystitis/bladder pain syndrome (IC/BPS). Animals exposed to water avoidance stress (WAS) have increased engagement of the brain micturition circuit. We evaluated the effect of voluntary exercise on the central amplification of stress-induced bladder hyperalgesia. After 10 days of WAS, W-K female rats were randomized to observation or daily exercise. Exercise animals had reduced bladder hypersensitivity, pain and frequency, with dose response. These changes correlated with brain changes in the micturition circuit (Barrington nucleus) and its control, the Periaqueductal Gray and the limbic system. **Conclusion:** Chronic exercise may help modify urinary symptoms in patients with IC/BPS.

