2016 ANNUAL MEETING HIGHLIGHTS
Female Urology/Incontinence

Course #028IC
Contemporary Pharmacotherapy for OAB

Course #033PG
Foundations of Female Urology

Course #046PG
Urodynamic Evaluation and Advances in Management of Adult Neurogenic Lower Urinary Tract Dysfunction in Adults: A Case Based Approach

Course #062IC
Botulinum Toxin: Why Use It, How to Do It, What are the Results?

Course #064IC
The Role of Sacral Neuromodulation in Urological Practice

Plenary Sessions
Panel Discussion: Management of Refractory OAB in the Geriatric Patient

Critical Discussion: Injection or Intestine: Management of the Hostile Neuropathic Bladder

Take Home Message: Female Urology/Incontinence/Urodynamics

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Publisher
American Urological Association
1000 Corporate Boulevard
Linthicum, MD 21090

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Educational grant support provided by:
- Allergan, Inc.
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2016 AUA Annual Meeting Highlights: Female Urology/Incontinence

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Estimated time to complete this activity: 1.25 hours
Release Date: October 2016
Expiration Date: October 31, 2017

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Statement of Need
Over the past several years there has been an evolution in the diagnosis and treatment of female urologic conditions such as stress urinary incontinence, pelvic organ prolapse and overactive bladder (OAB). Technological and pharmacological advances are constantly occurring. Thus there is an educational need for increased knowledge, particularly related to advances in the specialty and understanding of current guidelines for the management of patients with these conditions.

Target Audience
Urologists, urologists in training and non-physician providers involved in urology.

Course #028IC: Contemporary Pharmacotherapy for OAB

Learning Objectives
At the conclusion of this CME activity, participants should be able to:
• Understand the similarities and differences between the various oral pharmacotherapies for overactive bladder
• Review the principles of physiology and pharmacotherapy for currently available agents, including the antimuscarinics and beta-3 agonists
• Realize the importance of setting proper patient expectations regarding treatment of OAB and the potential need for sequential and even additive therapies
• Analyze the clinical (and theoretical) advantages and limitations of currently available agents
• Learn about potential future pharmacological pathways and therapies for OAB

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CME Information
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Course #033PG: Foundations of Female Urology

Learning Objectives
At the conclusion of this CME activity, participants should be able to:
• Cite the basic concepts of pelvic floor anatomy, and how certain defects cause pelvic organ prolapse
• Distinguish the different prolapse surgeries, and the certain types of pelvic floor defects they correct
• Interpret the latest concepts regarding the pathophysiology and surgical treatment of stress urinary incontinence, and integrate guidelines into clinical management
• Enumerate the basic principles of urodynamic testing in women with pelvic organ prolapse, and integrate guidelines into clinical management
• Incorporate the diagnosis and management of OAB, and integrate guidelines into treatment

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Course #046PG: Urodynamic Evaluation and Advances in Management of Adult Neurogenic Lower Urinary Tract Dysfunction in Adults: A Case Based Approach

Learning Objectives
At the conclusion of this CME activity, participants should be able to:
• Confidently evaluate urodynamically adult neurogenic lower urinary tract conditions
• Be proficient in the comprehensive, evidence-based, and contemporary management of neurogenic lower urinary tract conditions
• Obtain instruction on the currently accepted followup management of adult patients with neurogenic lower urinary tract conditions

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Course #062IC: Botulinum Toxin: Why Use It, How to Do It, What are the Results?

Learning Objectives
At the conclusion of this CME activity, participants should be able to:
• Cite the mechanism of action of botulinum toxin
• Describe the role of the toxin as a form of treatment for the bladder, sphincter and prostate
• Identify limitations and potential complications of botulinum toxin treatment
• Examine patient types who may benefit from treatment with botulinum toxin treatment
• Compare and contrast injection techniques

Faculty

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Learning Objectives

At the conclusion of this CME activity, participants should be able to:

• Summarize the basic elements of sacral neuromodulation (SNM)
• Translate the theory of neuromodulation to the pathophysiology of voiding dysfunction
• Differentiate when SNM may be appropriate for patients in clinical practice
• Review new and potential future indications and weigh therapeutic alternatives
• Exemplify troubleshooting and best practice techniques

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Acknowledgements

The AUA Office of Education would like to thank the companies who support continuing education of physicians. The AUA recognizes the following companies for providing educational grant support:

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Contemporary Pharmacotherapy for OAB

Eric Rovner, MD, Course Director; Christopher Chapple, BSc, MD, DHC, FRCS, FEBU and Alan Wein, MD, PhD (Hon), Faculty

This 2-hour course at the AUA meeting covered oral drug therapy for overactive bladder (OAB) with a particular view towards those compounds clinically in use as well as those in development. Guideline documents from AUA/SUFU (Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction) as well as the EAU (European Association of Urology) and ICI (International Consultation on Incontinence) were reviewed and summarized.

Patient expectations were discussed as they related to efficacy and adverse effects. It is critically important to provide accurate and realistic expectations of outcomes with OAB pharmacotherapy. There are many “measuring tools” for setting such expectations and goals including diary parameters, dry rates and patient reported outcome measures. Recently, self-reported and self-determined outcome measures, wherein the patient chooses his/her own goals for OAB pharmacotherapy have emerged.

The lower urinary tract is a complex organ. There is a close interaction between the afferent and efferent systems under the influence of which the effecter organ, the detrusor muscle, is responsible for storage of urine at low pressure, and its effective voiding at a convenient time and place. Disorders of the lower urinary tract can result from dysfunction at a number of levels, either peripherally affecting the sensory motor innervation or the detrusor muscle, or at the level of the central nervous system within the spinal cortex or cerebral cortex. It is now clearly established that sensory mechanisms are important in the genesis of normal bladder function, and disorders of innervation and function of the detrusor muscle can lead to significant lower urinary tract dysfunction.

The gold standard investigation of the lower urinary tract is a careful history and use of a bladder diary followed when necessary by pressure flow urodynamics, which represent the subjective interpretation of objective parameters. Conversely, symptom scoring is a valuable adjunct but represents the objective interpretation of subjective parameters, and it must be remembered that “the bladder is an unreliable witness.”

It is essential to evaluate the evidence base when considering the treatment of storage symptoms affecting the lower urinary tract, and in particular incontinence. Prof. Chapple drew heavily on work from the Cochrane Collaboration, the International Consultation on Urological Disease as well as the recent EAU Guidelines. The evidence base relating to investigative techniques, conservative management and intervention pharmacotherapy were reviewed in detail.

The overactive bladder as described several years ago represents a storage symptom complex characterized by the symptom of urgency. It occurs with increasing age in the population and in 40% to 60% of women and 60% to 90% of men, with or without incontinence. The normal sensory and motor control mechanism under which the bladder works underscores the potential for pharmacotherapeutic modulation of lower urinary tract function with reference to existing drug therapy, including anticholinergics, the beta-3 agonist mirabegron and onabotulinumtoxin A. Anticholinergic therapy has been used for many years, and the evidence base relating to this is critical in understanding what these drugs can and cannot do. Desmopressin has also been used, particularly in the context of management of nocturia.

Dr. Wein discussed potential management strategies for overactive bladder/detrusor overactivity and what the ideal drug for overactive bladder would accomplish, taking into consideration that one of the most important things is to adjust patient expectations on a realistic scale. The rationale for the use of antimuscarinics was discussed as well as the typical results to be expected from antimuscarinics in terms of urgency urinary incontinence reduction, urgency episode reduction, micturition frequency reduction and changes in quality of life assays. The adverse events were discussed in terms of dry mouth, constipation, possible cardiac side effects and cognitive side effects especially in the elderly.

The efficacy of combined behavioral and drug therapy for urgency urinary incontinence over the efficacy achieved with either alone was discussed. Some individual effects on urgency were discussed but only to point out that figures vary widely depending on exactly how “urgency” is quantitated or measured. The ICI assessments for various antimuscarinics and drugs with a combined action were presented as well as the ICI recommendation for the treatment of lower urinary tract symptoms with alpha1-adrenergic receptor antagonists. The EAU levels of evidence and grades of recommendation were also presented. Included was the topic of the use of antimuscarinics in men, the elderly and, separately, those with neurogenic detrusor overactivity. Discontinuation rates and the reasons for discontinuation were discussed. With respect to the beta-3 agonists (only 1 such agent is commercially available at present), recommendations made by the ICI and EAU were discussed along with efficacy figures for at least reduction in urgency incontinence episodes and micturition frequency.

The mechanisms to decrease nocturia were presented as well as the outcome indicators and the results of treatment with various antimuscarinic agents. The results were discussed with reference...
to why failure is the most common outcome with antimuscarinics or beta-3 agonists except in certain circumstances, and these were explained. Finally, the subject of comparison data for overactive bladder treatment was presented. The overriding concept is always uroselectivity, as originally defined by Anderson. The concept of real and theoretical edges was discussed as well as the possible difference between statistical and clinical significance.

The subject of combination therapy is clearly topical at present and carries with it the potential for introducing the therapeutic benefit with any individual agent, but also as a downside it introduces the side effect profile seen with any specific agent. This needs to be understood with reference to existing therapies for the management of lower urinary tract symptoms in males and females. The potential roles of combination therapies are legion and include hormonal agents, combination therapy with beta-3 agonists and antimuscarinics, the potential for management of storage symptoms in the male by adding botulinum toxin and other toxins, and combinations of alpha blockers + 5-alpha reductase inhibitors, alpha blockers + antimuscarinics and the use of phosphodiesterase type 5 inhibitors potentially coupled with alpha blocker therapy or 5-alpha reductase inhibitors.

Finally, the possibilities for future pharmacological therapy for overactive bladder were presented. Potential management strategies were discussed as well as the main problem, which is always uroselectivity. New ideas regarding antimuscarinic and beta-3 adrenoceptor agonists were presented. Negative findings or comments regarding potassium channel openers, calcium channel antagonists and prostaglandin receptor antagonists were presented, and “positive” results with comments were discussed with respect to duloxetine, COX inhibitors, vitamin D-3 agonists and neurokinin receptor antagonists. Promising animal data with respect to GABAB receptor agonists and purinergic receptor antagonists were described as well as for cannabinoids, TRP antagonists and opioid receptors. The concept of combining drugs and also for combining drugs with other forms of treatment was discussed.

**Course #028IC**

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**Course #033PG**

**Foundations in Female Urology**

J. Christian Winters, MD, FACS, Course Director; Stephen R. Kraus, MD and Nirit Rosenblum, MD, Faculty

This highly interactive course was designed to provide the practitioner with an introduction into the specialty of female urology. Session 1 was devoted to urodynamic testing in women and stress urinary incontinence (SUI), session 2 focused on pelvic organ prolapse (POP), and session 3 included lectures on overactive bladder (OAB) guidelines and complications occurring after transvaginal surgery with pearls for management. Each session included a didactic lecture followed by video demonstrations and a question and answer period.

The course began with an overview of urodynamic testing in women by Dr. Kraus. The importance of adhering to good urodynamic practice, specifically formulating the urodynamic questions before the study, was emphasized. The clinician should have an idea of precisely what data are needed from the urodynamic exam based on the history and physical examination as well as other ancillary tests. Proper urodynamic technique, patient positioning, zeroing the transducers to atmospheric pressure, and measuring the leak point pressures correctly were reviewed. When zeroing the transducers to the atmospheric pressure, the transducers are placed at the level of the pubic symphysis and the tubing is “zero” calibrated to atmospheric pressure before connecting to the urodynamic catheters. With this technique, baseline abdominal and intravesical pressures are never zero. The urodynamic findings of poor compliance were reviewed and differentiated between abdominal and Valsalva leak point pressures. Examples of each were demonstrated along with how SUI is diagnosed and characterized by the abdominal leak point pressure. An overview of the pertinent AUA guidelines on adult urodynamics was presented.

Dr. Rosenblum followed with a discussion of the pathophysiology and treatment of SUI, providing great detail about the anatomy of urethral support. Defects in urethral support may lead to urethral hypermobility and pose to SUI. However, not all women with hypermobility leak urine and it appears that any woman with SUI must have some degree of intrinsic sphincter deficiency. The standard evaluation of history and physical examination, stress test, urinalysis, post-void residual and assessment of bother was outlined for the audience.

The “acceptable” surgical procedures for SUI were reviewed, which include retropubic suspension, pubovaginal sling, mid urethral sling (MUS) and urethral injection therapy. The declining numbers of Burch procedures being done was noted, but it was reaffirmed that in women with urethral hypermobility undergoing abdominal surgery these operations may still be performed successfully. However, most in the audience agreed that even in this setting they would still proceed to MUS, and the best outcomes data in the surgical management of SUI are for sling procedures. Slings have the highest degree of efficacy but it must be noted that MUS proce-
dures have efficacy similar to that of the pubovaginal sling with less perioperative morbidity.

Following these comprehensive lectures, videos of the retropubic and obturator MUS as well as the pubovaginal sling procedures were reviewed with the audience. Many in the audience remain quite concerned about the controversy surrounding the MUS, and the entire faculty noted their preferential use of the retropubic MUS. It was also pointed out that use of the sling is highly recommended by SUFU, the AUA and many other subspecialty societies involved in female pelvic surgery.

Dr. Winters reviewed normal pelvic anatomy and then defined the various defects creating the prolapse conditions physicians most commonly treat. The etiology of POP is multifactorial, ranging from childbirth to disorders of connective tissue. The commonly performed prolapse procedures and vaginal support defects they correct were illustrated. The importance of the apex in vaginal support was noted and it was emphasized that when present, apical support defects must be corrected to achieve successful outcomes. Instructional videos on abdominal sacrocolpopexy, transvaginal prolapse correction and colpocleisis procedures were presented.

The course concluded with lectures on OAB and its management. The AUA/SUFU guideline on the evaluation and management of OAB was reviewed, and it was stressed that in most uncomplicated cases, proceeding to first and/or second line therapies is preferred over urodynamics and more extensive evaluation methods. In the final lecture the most common presentations of transvaginal mesh surgery were described along with illustrated principles guiding surgical management. For erosions in the bladder, minimally invasive techniques are still feasible and their application is at the discretion of the surgeon. At all times, surgeons should adhere to sound reconstructive principles. Early intervention for women who are in retention following MUS was emphasized, and there is no need to wait as is commonly done for pubovaginal sling procedures. To conclude, participants were guided through various clinical scenarios in the area of female urology. A question and answer period then completed this dynamic and highly interactive session, which was designed to provide participants with an introduction to the principles and practice of female urology. The audience complimented the instructional videos in each of the sessions, which emphasized the teaching points and were likely to facilitate their future practice.

Urodynamic Evaluation and Advances in Management of Neurogenic Lower Urinary Tract Dysfunction in Adults: A Case Based Approach

Hari Tunuguntla, MD, MS, MCh, Course Director; Angelo E. Gousse, MD and Stephen R. Kraus, MD, Faculty

Introduction

Neurogenic lower urinary tract dysfunction (NLUTD) is a disorder of the lower urinary tract secondary to disease of the nervous system. This disease process can cause dysfunction of bladder storage and/or emptying with significant clinical, social and economic implications for the patient, caregiver and health care system. Timely diagnosis of NLUTD and appropriate management are imperative to prevent potentially irreversible upper urinary tract deterioration and adverse outcomes especially in patients with high risk features, ie high detrusor leak point pressures and/or low detrusor compliance. Some of the conditions resulting in high risk NLUTD include spinal cord injury (SCI), advanced multiple sclerosis and spina bifida. Such patients are at increased risk for renal failure, nephrolithiasis, vesicoureteral reflux (VUR) and urinary tract infections (UTI)/urosepsis. Patterns of Voiding Dysfunction

Neurological disorders that cause NLUTD can be classified by location of the lesion, which will aid in predicting the type of clinical/urodynamic abnormality as well as assist in prognostication and formulating treatment strategies. These disorders are classified as suprapontine, infrapontine-suprasacral, sacral and peripheral lesions. Such a classification helps to predict the type of clinical/urodynamic abnormality, and has therapeutic and prognostic significance. Characterization of the lower urinary tract dysfunction as failure to store and failure to empty has therapeutic significance.

Evaluation

A thorough history and physical examination are necessary in the evaluation of patients with NLUTD to understand the functional abnormality (failure to store vs failure to empty). The upper urinary tract should be evaluated anatomically and functionally. The upper urinary tract is assessed by renal ultrason sound or computerized tomography for upper urinary tract anatomy, renal function profile including glomerular filtration rate, and nuclear renal scan to assess renal function and rule out
obstructive uropathy. Lower urinary tract evaluation consists of bladder ultrasound, (video)urodynamic study (UDS), cystogram to rule out VUR and cystoscopy to assess the urethra, bladder outlet, prostate and bladder.\(^5\) Initial evaluation of the patient with NLUTD includes baseline UDS and renal/bladder ultrasound.

**Urodynamic Evaluation**

UDS is a dynamic/functional assessment of the lower urinary tract by evaluating the storage and evacuation of urine which aids in the identification of those patients at risk for upper tract deterioration. Urodynamic risk factors include high detrusor filling pressures, low detrusor compliance, detrusor leak point pressure greater than 40 cm H\(_2\)O and detrusor external sphincter dysynergia (DESD). Videourodynamic study is useful to evaluate the bladder neck, detrusor sphincter dyssynergia and anatomical abnormalities in the lower urinary tract; to assess for trabeculated bladder and bladder diverticula; and to document VUR.\(^3\)\(^6\)

Suprapontine lesions such as cerebrovascular accident and brain tumors are associated with detrusor overactivity (DO) with synergic sphincter.\(^7\) Infra-pontine-suprasacral spinal cord lesions such as spinal cord injury, multiple sclerosis, spina bifida and others exhibit upper motor neuron bladder dysfunction including detrusor overactivity and DESD.\(^4\) These patients are at potential risk for upper tract deterioration secondary to DESD.\(^8\) Sacral lesions and peripheral nerve lesions manifest with hypocontractile or areflexic detrusor. Sacral lesions can present with various urodynamic abnormalities. The external sphincter can remain functional with sacral neurological lesions and contributes to bladder overdistention.\(^9\) Lesions that damage the detrusor nucleus but spare the pudendal nucleus pose a mixed picture resulting in an acontractile detrusor and a hypertonic external sphincter ultimately leading to urinary retention.\(^4\) Lumbar disk herniation presents with acontractile detrusor in about 65% of patients.

Sacral spinal cord injury also results in acontractile bladder. The external sphincter usually remains functional at this level, which may contribute to bladder over distention. Mixed type B NLUTD may result from sacral spinal cord lesions that spare the detrusor nucleus but damage the pudendal nucleus, resulting in a flaccid external urinary sphincter but a spastic bladder secondary to detrusor over activity with possible urinary incontinence.\(^4\) Voiding dysfunction after radical pelvic surgery is commonly seen after abdominoperineal resection and radical hysterectomy, and occurs in 10% to 60% of these patients. Patients initially present with urinary retention secondary to hypocontractile detrusor and stress urinary incontinence due to the open and fixed external urethral sphincter. Urodynamic findings include decreased compliance, open bladder neck and fixed striated sphincter.

**Management**

The management of NLUTD depends on clinical presentation, level of neurological injury and patient preference. Failure to empty is managed by clean intermittent catheterization (CIC), indwelling transurethral catheter or indwelling suprapubic cystotomy catheter.\(^3\) Behavioral treatment is useful for patients with incomplete spinal lesions who retain filling sensation and can be accomplished by timed voiding.\(^10\) Patients with detrusor overactivity and/or decreased compliance are treated with antimuscarinics to prevent possible upper urinary tract damage. Oral medication is used as first line therapy. If unsuccessful, bladder chemodenervation with onabotulinumtoxinA (onabotNTA) is a minimally invasive treatment option for patients with detrusor overactivity, and has been shown to significantly improve mean number of incontinence episodes as well as certain urodynamic parameters. onabotNTA can also be used for chemodenervation of the external urinary sphincter in patients with detrusor sphincter dys-synergia.\(^3\)\(^,\)\(^11\)\(^,\)\(^12\)

Surgical management is indicated for patients with high risk NLUTD refractory to conservative and minimally invasive (eg bladder chemodenervation) treatments. Augmentation cystoplasty is an option for patients with DO, poor detrusor compliance and intractable incontinence. Bladder augmentation increases bladder capacity, reduces intravesical pressure and protects the upper urinary tract. Retrospective analysis revealed a mean bladder capacity increase from 115 mL to 513 mL with about 75% of patients requiring CIC.\(^3\)\(^,\)\(^13\) Long-term risks of augmentation include bladder stones, UTI and metabolic abnormalities.\(^3\) Urinary diversion with an ileal conduit with or without cystectomy as a definitive treatment option for NLUTD provides continuous drainage of urine and may be considered for patients with decreased compliance, upper tract deterioration and severe incontinence and/or recurrent UTI wishing to be catheter-free.\(^3\)

Bladder emptying can be facilitated by external urethral sphincterotomy in patients with DESD, recurrent UTI secondary to failure to empty the bladder, autonomic dysreflexia or ineffective CIC. This procedure relieves autonomic dysreflexia in patients with lesions above T6 who are unable to perform catheterization.\(^3\)\(^,\)\(^14\)

Patients with neurogenic stress urinary incontinence have various treatment options depending on gender. Female patients can be offered transurethral bulking agent injection, pubovaginal sling, mid urethral sling and bladder neck closures with urinary diversion, whereas males are treated with urethral sling or artificial urinary sphincter. Close followup is indicated in these patients to detect a high pressure bladder.\(^3\) Bladder neck closure is useful in patients with an unsalvageable urethra.

**Followup**

Regular and close followup of patients with NLUTD is required. However, there is no consensus on the type of evaluation or frequency of followup.
The Consortium of Spinal Cord Medicine guidelines suggest patients with SCI undergo an annual urological evaluation. Annual history and physical examination with lab values assessing renal function should be obtained. Abrams et al suggest imaging of the upper and lower urinary tracts with ultrasound, monitoring renal function and urodynamics as indicated when new deteriorating symptoms present at 6 months, 12 months, then annually. UDS is repeated every 5 to 10 years as clinically indicated. The AUA/SUFU guidelines recommend pressure flow study or multichannel cystometrogram for patients with any relevant neurogenic conditions regardless of symptoms as monitoring for symptoms alone may miss treatment failures. Patients with NLUTD should undergo UDS at diagnosis and at followup. The EAU outlined a risk adapted followup for patients with NLUTD (see Appendix).

Conclusions

A comprehensive evaluation is important to formulate an effective and individualized treatment plan for patients with NLUTD. High risk groups at risk for upper urinary tract deterioration include patients with spinal cord injury, advanced multiple sclerosis and spina bifida. All patients should undergo a thorough history and physical examination with a baseline renal/bladder ultrasound as well as UDS. The goal of managing NLUTD is to preserve the upper and lower urinary tracts from any damage. Spinal cord lesions above T6 may be associated with autonomic dysplasia. Myelodysplasia is associated with an open and fixed sphincter. Patients should be frequently monitored given that they are predisposed to nephrolithiasis, UTI/urosepsis and upper tract deterioration. A risk based and patient oriented approach combined with regular followup can improve outcomes and quality of life by preventing complications. UDS should be obtained at diagnosis and at followup. Clinical symptom based followup alone may miss treatment failures.

Acknowledgement. Dr. Kashan Radadia assisted with writing this summary.

Appendix

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Level of Evidence</th>
<th>Grade of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk patients: assess upper urinary tract Q6 months</td>
<td>4</td>
<td>A</td>
</tr>
<tr>
<td>High risk patients: physical exam, urinalysis every year</td>
<td>4</td>
<td>A</td>
</tr>
<tr>
<td>Any significant clinical changes indicate further specialized evaluation</td>
<td>4</td>
<td>A</td>
</tr>
<tr>
<td>UDS mandatory at baseline and should be done at regular intervals</td>
<td>3</td>
<td>A</td>
</tr>
</tbody>
</table>

for the treatment of refractory bladder dysfunction. Years of research by many people led to 2 approved urological indications for BoNT in the United States. 1) In 2011, 200 U onabotulinumtoxinA (onaBoNTA) were approved for the treatment of urinary incontinence due to detrusor overactivity associated with a neurological condition in adults who had an inadequate response to or were intolerant of an anticholinergic medication. 2) In 2013, 100 U onaBoNTA were approved for the treatment of overactive bladder (OAB) with symptoms of urinary incontinence, urgency and frequency in adults who had an inadequate response to or were intolerant of an anticholinergic medication.

In this AUA course the participants and I had a lively discussion of the practical aspects of the who, when and how of bladder BoNT injection. The course included case studies, a video presentation and open dialogue with questions and answers.

**Patient Preparation**

Urinalysis should be checked at the time of the procedure (if the patient has a history of chronic bacteriuria, appropriate preoperative antibiotic coverage is indicated). Anticoagulation medicine should be stopped temporarily and informed consent obtained. The bladder should be empty and local anesthesia should be applied (1% lidocaine) with or without sedation. The bladder should be partially filled to approximately 150 to 200 ml for visualization but over distention should be avoided. Latex allergy precautions should be considered in the population at risk for NDO. In spinal cord injured patients or even possibly those with multiple sclerosis with injury and/or lesions above T6, precautions to deal with and procedures to minimize the risk of autonomic dysreflexia should be in place.

**Injection Paradigm**

For NDO the recommended dose is 200 U onaBoNTA, the recommended reconstitution volume is 30 ml sterile injectable saline, volume per injection is 1 ml, depth of injection is 2 mm intra-detrusor and injections are 30 sites spaced approximately 1 cm apart starting 1 cm above the trigone. For idiopathic OAB the recommended dose is 100 U onaBoNTA reconstituted in 10 ml saline and injected into 20 sites at 0.5 ml per site.

**Cystoscopic Techniques**

Flexible and rigid cystoscopic techniques work well for BoNT injection. Surgeon preference and institutional practice usually affect the decision of what technique is used (see figure). Flexible cystoscope. I use flexible cystoscopy in the office in the majority of men and women. The flexible scope accommodates a 27 gauge 4 mm long flexible injection needle. Office procedures with only local anesthesia are adequate for most patients and they appreciate the convenience of an office procedure.

**Rigid cystoscope.** A rigid scope with a 12 or 30-degree lens bridged with an accessory working element loaded with a 25 gauge needle is recommended. The rigid scope allows for easier orientation within the bladder compared to a flexible cystoscope, the working element facilitates rapid injection into the bladder, and the 25 gauge needle minimizes bleeding and potential backflow from the injection sites. The bladder volume is typically kept at 150 to 200 ml, and blood vessels are avoided during injection.

**Figure.** onaBoNTA is administered via rigid or flexible cystoscopic techniques starting above trigone to depth of approximately 2 mm. Reprinted with permission.²

**Mixing the Toxin**

Each vial of 100 U onaBoNTA comes in a 10 ml bottle. I do not reconstitute the toxin until I know that infection has been ruled out or an appropriate antibiotic started to avoid waste. The onaBoNTA vials should be stored in the refrigerator at 2C to 8C (36F to 46F). After reconstitution, the vials may be stored in the refrigerator for up to 24 hours. onaBoNTA should be used immediately after reconstitution and should not be stored in the syringe. Typical doses in adults treated with abobotulinumtoxinA or rimabotulinumtoxinB range between 500 and 1,000 U, and 2,500 and 15,000 U (ie 5,000 U is most common), respectively.

**Followup**

I instruct patients that they may notice some pain and blood tinged urine, as well as possible difficulty urinating after treatment, which should resolve within 24 to 48 hours, but they should contact my office if they have any questions or concerns. I discuss the appropriate antibiotic coverage and risk of infection with these patients who often have bladder infections. It may take several days to notice a gradual improvement in OAB symptoms. Similarly, it generally takes several days for a patient to notice impaired voiding and I instruct that patient to start self-catheterization if clinically necessary. Office followup in about 2 weeks with urinalysis and post-void residual urine measures is recommended.

**How Long Does it Last?**

It generally takes about 1 to 2 weeks for patients to notice some relief of symptoms. If the injection helps, he or she will experience further improvement that usually reaches a maximal benefit at about 1 month. The beneficial effect is usually maintained for 6 to 9 months. Subsequently, urination or catheterization frequency starts to increase and incontinence recurs. These are signals...
I tell patients to look for and to contact my office to schedule repeat injections. I wait 3 months before reinjections even if patients report partial improvement and request repeat injections sooner. One warning is not to inject more than a total of 400 U onaBoNTA in any part of the body in a 3-month period. This precaution is important if the patient is receiving BoNT injection by another physician to a different part of the body.

Subsequent Injection

For the majority of patients who notice a benefit with bladder BoNT therapy, I use the same dose with repeat injections. Most of the neurologically impaired patients have had consistent improvement using the same dose for more than 15 years. If the patient finds benefit but incontinence did not adequately resolve with 100 U onaBoNTA, I may consider increasing the dose to 150 or 200 U onaBoNTA at the next injection. Alternatively, in patients with NDO who do not perform self-catheterization but have noticed retention or incomplete bladder emptying, I generally start at 100 U onaBoNTA. Dose titration is possible and helpful but in my experience the percentage of patients who will need dose adjustment up or down is small.

Risk of Antibody Formation

Failure to respond to BoNT injection might result from the presence of preexisting or formation of BoNT antibodies. The incidence of onaBoNTA antibody formation is only about 1%. I have not had a case of documented positive BoNT antibodies since I first used BoNT in 1998 and I generally perform the frontalis antibody test for clinical confirmation when a patient reports that BoNT is not working after previous successful injections.

What are the Results?

Neurogenic indication. The neurogenic detrusor overactivity indication received regulatory approval in 2011. A total of 691 patients with spinal cord injury or multiple sclerosis who had an inadequate response or were intolerant of 1 or more anticholinergic medications were enrolled in phase 3 studies. These patients were randomized to receive 200 U onaBoNTA (227 patients), 300 U onaBoNTA (223) or placebo (241). In both studies significant improvement in the primary efficacy variable of change from baseline in weekly incontinence episode frequency was achieved with 200 U onaBoNTA compared with placebo. The 300 U dose was not better than 200 U but had more side effects. onaBoNTA treatment was associated with significant improvements in maximal cystometric capacity of approximately 150 ml. Among patients who were not catheterizing at baseline before treatment, catheterization for urinary retention was initiated in 30.6% after treatment with 200 U onaBoNTA vs 6.7% of those on placebo. The most frequently reported adverse reactions within 12 weeks included urinary tract infection (24%), urinary retention (17%), hematuria (4%), fatigue (4%) and insomnia (2%).

Idiopathic indication. onaBoNTA received regulatory approval for idiopathic detrusor overactivity in 2013. Phase 3 studies demonstrated the safety and efficacy of onaBoNTA in patients with OAB whose symptoms were not adequately managed with anticholinergic medications. onaBoNTA reduced the daily frequency of urinary leakage episodes from baseline by approximately 50% or more by week 12 compared to placebo (reduction of 2.5 episodes from baseline of 5.5 in study 1 and reduction of 3 episodes from baseline of 5.5 in study 2 for those treated with onaBoNTA vs a reduction of 0.9 episodes from a baseline of 5.1 in study 1 and a reduction of 1.1 from a baseline of 5.7 in study 2 for those treated with placebo). The efficacy of onaBoNTA in reducing urinary leakage and other OAB symptoms was up to 6 months in duration. Urination frequency and the amount of urine voided also improved with onaBoNTA treatment compared to placebo at week 12. The most common side effects reported with onaBoNTA in clinical studies were urinary tract infection (18% vs 6% with placebo); dysuria (9% vs 7% with placebo), which means painful or difficult urination; and urinary retention (6% vs 0% with placebo), which is a temporary inability to fully empty the bladder requiring clean intermittent catheterization. Urinary retention was more likely to develop in patients with diabetes mellitus treated with onaBoNTA.

Considerations for Safe Clinical Use of Botulinum Toxin

- Health care professionals should be aware that a boxed warning is part of the prescribing information of botulinum toxin in the United States to highlight that BoNT may spread from the area of injection to produce systemic effects consistent with botulism.
- Symptoms such as unexpected loss of strength or muscle weakness, hoarseness or trouble talking (dysphonia), trouble saying words clearly (dysarthria), loss of bladder control, trouble breathing, trouble swallowing, double vision, blurred vision and drooping eyelids may occur.
- Understand that swallowing and breathing difficulties can be life threatening, and there have been reports of deaths related to the effect of spread of BoNT.
- Be aware that children treated for spasticity are at greatest risk for these symptoms but symptoms can also occur in adults treated for spasticity and other conditions.
- Realize that cases of toxin spread have occurred at BoNT doses comparable to those used to treat cervical dystonia and at lower doses.
- Understand that BoNT products are not interchangeable and that the established drug names of the BoNT products have been changed to emphasize the different dose-to-potency ratios of these products. The doses expressed in units are not comparable from 1 BoNT product to the next. Units of 1 product
cannot be converted into units of another product.


The Role of Sacral Neuromodulation in Urological Practice

Steven W. Siegel, MD, Course Director

Patients with an overactive bladder (OAB) related diagnosis comprise a large percentage of visits to the general urology practice. Many patients do not experience sufficient improvement with behavioral and/or drug treatments, which comprise first and second line therapies according to AUA guidelines. There is a high discontinuation rate noted among patients treated with anticholinergic agents, primarily due to incomplete symptom control balanced against cost and side effects, including dry mouth and constipation. Younger patients are especially likely to find drugs intolerable for these reasons. A beta-3 agonist is an alternative that will help some patients who would otherwise not benefit from medications alone. Yet we have found that a surprisingly small percentage of our patients in a large group practice receive anything other than medications for OAB complaints, and an even smaller group goes on to advanced treatment or third line therapy.

Third Line Therapies

An increasing number of options can be used as a compliment or alternative to anticholinergic drugs, such as sacral neuromodulation (SNM), percutaneous tibial nerve stimulation (PTNS) and intravesical botulinum toxin (BoNT). Which one to choose? I use all of them depending on the situation. This course presumes the more conservative or first and second line options have been insufficient. Use of sacral neuromodulation in patients who do not respond adequately, and the positioning of SNM relative to PTNS and BoNT are discussed.

Sacral Neuromodulation

SNM involves chronic modulation of S3 and less frequently, S4 via a percutaneous route. Modulation implies the therapy is thought to act indirectly via a central afferent mechanism, targeting reflex centers in the spinal cord and pons, and influencing reflexes among the bladder, urethral sphincter and pelvic floor. Stimulation implies a more direct effect on efferent motor neurons as in functional electrical stimulation.

The therapy, marketed internationally as InterStim®, uses an implantable system including a lead electrode and an implantable neurostimulator (INS). There is typically a trial or screening phase using a percutaneous lead lasting for 3 to 7 days (percutaneous nerve evaluation) or a staged lead implant when the chronic lead is implanted surgically. The therapy may be trialed for up to several weeks and, if successful, the lead may then be converted for long-term use by connecting it to an INS.

Present and Future Indications for SNM

The FDA (U.S. Food and Drug Administration) approved SNM for patients with refractory OAB and idiopathic, nonobstructive urinary retention (NOUR). SNM is also approved for urinary incontinence due to neurogenic detrusor overactivity: a randomised, double-blind, placebo-controlled trial. Eur Urol 2011; 60: 742.


Recent publication of the InSite trial revealed SNM to be superior to anticholinergics after an inadequate response to 2 drugs, and at 12 months it remained safe and effective. There have been hundreds of other publications in the peer reviewed literature regarding SNM. In general, randomized controlled trials/case series indicate an approximately 80%/70% success rate, defined by at least a 50% decrease in relevant voiding parameters. Studies also demonstrate significant improvement in quality of life, decreased use and cost of therapeutic alternatives, and long-term benefit.
These results were underscored in the recently published 3-year InSite study data, demonstrating OAB therapeutic success in 83% of patients at 36 months. The benefits involving quality of life were also dramatic and maintained. The 60-month data will soon be available for report.

The degree of improvement, even among the patients with the most severe baseline symptoms, has been shown to be greater than among patients successfully treated in OAB drug trials (based on package inserts/FDA submitted trials). Similarly, the degree of improvement seen in patients treated with PTNS appears to be about half as much as in patients who are less symptomatic initially. Randomized head-to-head trials have not been reported.

**SNM vs BoNT or PTNS**

Much discussion has been focused on the relative merits of intravesical BoNT vs SNM in urology patients. I use both in my practice, and believe that the therapies have different strengths and weaknesses which should be considered when discussing with patients (Appendix 1). In general, patients with significant bowel symptoms, pelvic pain and nonobstructive urinary retention are more likely to benefit from SNM, while elderly patients, those with progressive neurogenic bladder, those likely to need body magnetic resonance imaging (MRI) or those in whom a trial of SNM has failed are more ideally suited for BoNT.

Unlike BoNT, there is likely to be a benefit from PTNS for bowel symptoms. Patients with demonstrable detrusor overactivity on urodynamic study, including those with more severe symptoms, are likely to experience a greater benefit from SNM than PTNS. Equivalent long-term efficacy of PTNS vs SNM has not been demonstrated, and there has not been a study conclusively indicating that the outcome of PTNS predicts the outcome of SNM. Of course, patient preference is paramount in choosing among these options.

**Troubleshooting SNM**

Typical problems encountered with SNM are summarized in Appendix 2. Recent studies have demonstrated a reoperation risk due to complications of less than 20% using modern techniques. There are several troubleshooting tips for dealing with common dilemmas.

**Infection prevention.** In a recent multicenter study the rate of infection of SNM devices was 3.4%. Perioperative antibiotics, similar to those used with other urological prosthetics, are a must. A Sage Cloth® is used to wipe the skin preoperatively. Patients shower preoperatively with Hibiclens®, and alcohol and Duraprep™ are used intraoperatively. Other intraoperative considerations include the use of an Ioban™ drape, making sure the incision is sufficiently deep, the lead extension tunnel is as long as possible during a staged trial and the excess lead is handled in a way to allow normal apposition of subcutaneous tissues. Evidence of a chronic, draining sinus is typically associated with implant infection. Once infection is obvious, all implanted components and the surrounding capsule must be removed, and incisions are allowed to heal (usually 3 months) before reimplantation, if elected.

**Lead problems.** Lead migration or lead fracture can cause decreasing efficacy. A fall or trauma is often responsible for these issues. Impedances greater than 4,000 Ω at 1 or more sites are indicative of fracture, while less than 50 Ω or equalization of impedances implies fluid in a connection site. Anteroposterior and lateral sacral films can be helpful in identifying these issues. While lead migration is rare, forward migration can occur in thin patients who had a “knuckle” of lead in the presacral area. Care to lay the lead down flat beneath the skin (by making a larger than normal or a “skipping” incision) can prevent this complication.

**Pain at INS site.** Using the small INS making a deep pocket parallel to the skin surface, just large enough to fit the device, and with careful hemostasis can be helpful in avoiding INS pain. It is important to place the device below the PSIC and lateral to the sacral edge to prevent direct compression over bone.

**Pregnancy.** While there is no direct evidence of problems from SNM during pregnancy, it is recommended that the device be turned off throughout term or as soon as pregnancy is known. Some patients may refuse because of the return of severe symptoms. In general, limitation of use during the first trimester and turning down stimulation levels are prudent steps. I believe an elective cesarean section should be considered by patients treated with SNM who have demonstrated pelvic floor hypertonus.

**MRI with SNM.** Most patients with intact systems using InterStim II INS can undergo MRI of the head or extremities only when using a send and receive MRI coil. The current SNM devices are not fully MRI compliant and axial MRI remains contraindicated. It is the lead and not the generator that represents the greatest risk to the patient during these studies. A connected lead is safer than a disconnected lead. Care should be taken to remove the entire lead when necessary and patients should be informed of retained leads. Careful counseling and informed consent are needed if MRI is considered for patients treated with SNM.

**Conclusions**

Urologists commonly care for patients with drug refractory voiding complaints. First line alternatives include behavioral therapy, biofeedback and physical therapy. Other options including SNM, PTNS and intravesical BoNT are important considerations for optimal benefit. The techniques, patient selection guidelines and troubleshooting measures discussed should help achieve a successful outcome.
Appendix 1

<table>
<thead>
<tr>
<th>Neuromodulation</th>
<th>Neurotoxin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Restores function</td>
<td>Takes it away</td>
</tr>
<tr>
<td>Treats retention</td>
<td>Causes it</td>
</tr>
<tr>
<td>Improves GI symptoms</td>
<td>No potential</td>
</tr>
<tr>
<td>WYSIWYG</td>
<td>Commits to 6-9 mo.</td>
</tr>
<tr>
<td>Use BoNT if fails</td>
<td>9 months before SNM</td>
</tr>
<tr>
<td>Long term benefit</td>
<td>Temporary</td>
</tr>
<tr>
<td>Infrequent reoperation</td>
<td>Frequent retreatment</td>
</tr>
</tbody>
</table>

Appendix 2

Common Problems

- Lack of or declining efficacy
- Wound complications/infection
- Painful stimulation
- Pain at IPG site
- Need for MRI
- Pregnancy
- Retained lead remnant
Panel Discussion: Management of Refractory OAB in the Geriatric Patient

David A. Ginsberg, MD, Moderator; Ragi Doggweiler, MD, Michael Albo, MD and Kenneth M. Peters, MD, Panelists

Overactive bladder (OAB) is a highly bothersome condition present in 30% to 35% of geriatric (defined as age 65 years or older) adults. According to the AUA, first and second tier treatments for OAB include behavioral and oral therapy, respectively. Behavioral therapy can be a challenge in older patients, as many have multiple comorbidities and are already taking multiple medications. Polypharmacy can be an especially worrisome issue in this population with possible drug-drug interactions as well as the possibility of an increased antimuscarinic load and increased risk of side effects related to other medications with antimuscarinic properties. The concerns of “anticholinergic load” are reflected in a recently published article that noted an association between antimuscarinic use and brain atrophy, cognitive dysfunction and clinical decline. While this is a single study of 52 patients, this side effect is something to keep in mind when treating OAB in older patients. Lastly, long-term adherence to medications is an issue for antimuscarinics and beta-3 agonists in all populations, including the elderly. Therefore, it is important to understand OAB treatment options beyond oral medications in this population. Third tier therapeutic options after failed first and second tier therapy for OAB include botulinum toxin, sacral nerve stimulation (SNS) and percutaneous tibial nerve stimulation (PTNS). This discussion focused on treatment options for the geriatric patient with refractory OAB.

Dr. Doggweiler reviewed outcomes with onabotulinumtoxinA (onaBoNTA). Numerous trials have shown onaBoNTA to be successful treating bothersome symptoms of OAB but few studies have focused on outcomes in

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Less than 65</th>
<th>65-74</th>
<th>75 or More</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy</td>
<td>100 U onaBoNTA</td>
<td>Placebo</td>
<td>100 U onaBoNTA</td>
</tr>
<tr>
<td>No. pts</td>
<td>344</td>
<td>348</td>
<td>169</td>
</tr>
<tr>
<td>No. UTI (%)</td>
<td>73 (21)</td>
<td>23 (7)</td>
<td>51 (30)</td>
</tr>
<tr>
<td>No. urinary retention (%)</td>
<td>21 (6)</td>
<td>2 (0.6)</td>
<td>14 (8)</td>
</tr>
</tbody>
</table>

Dr. Albo discussed the outcomes of patients undergoing SNS and PTNS. Neuromodulation is defined as the physiological process by which the influence of activity on a neural pathway modulates the preexisting activity in another pathway through synaptic interaction. SNS and PTNS share a common mechanism of action thought to involve activation of somatic afferent nerves projecting into the lumbosacral nerve plexus which then modulate either sacral reflex centers or suprasacral messaging in the central nervous system (CNS) centers involved with bladder control. In fact, there are reasons to believe that these therapies are optimal in the geriatric population based on this mechanism of action.

Neuroimaging techniques have demonstrated a relationship between aging and decreased lower urinary tract sensory feedback to the CNS and loss of intracerebral connectivity between the centers important for bladder control. Interestingly, these are the areas in the CNS affected by neuromodulation. In addition, neuromodulation avoids the side effects and drug-drug interactions that can occur with oral medications, avoids the possible need for CIC associated with onaBoNTA and can potentially treat concomitant conditions such as fecal incontinence.

Continued on page 16
While the initial data indicated that neuromodulation was less effective in the elderly, more recent data suggest otherwise. Peters et al analyzed a cohort of 300 patients treated with SNs divided into 3 age groups (less than 40 years, 40 to 64 years and 65 or greater years) and found no difference in symptom improvement or complication rates among the 3 groups.\(^{14}\) In addition, a number of studies have demonstrated that age is not a predictor of success after treatment with PTNS.\(^ {15,16}\) However, there also may be unique challenges implementing neuromodulation in this patient population. First, PTNS requires 12 weekly office treatments and, if successful, monthly treatments to maintain a response. While some patients like the idea of a regular office visit, frequent transportation of the geriatric patient may not always be feasible. SNS is implanted in the operating room and requires anesthesia at the time of initial implant and at the time of any revision/battery replacement. Comorbidities may limit this option for patients who may be considered an anesthesia risk (or refuse an option that requires anesthesia).

Dr. Peters concluded the session with a discussion of new technologies. This peek into the future is hopefully a preview of therapies that we will soon have available to treat OAB and be especially helpful for the geriatric patient with refractory OAB.

Clinical trials are currently under way to implant a wireless tibial nerve electrode in the office setting. This electrode would be powered by an external energy source allowing patients to stimulate the tibial nerve as needed to control symptoms, which would allow for neuromodulation while at the same time minimize some of the potential challenges that PTNS (need for multiple office visits) and SNS (need for placement of the device in the operating room) have in the elderly population.

Another potential exciting new twist of a presently used therapy is liposomal botulinum toxin. Liposomal botulinum toxin allows for the delivery of the drug in the office as an intravesical instillation without the need for cystoscopic injection. Results from a recent, randomized trial revealed reduction in urinary frequency and urgency, and no evidence of urinary retention.\(^ {17}\) Liposomal botulinum toxin currently is in clinical trials and may be an ideal treatment for the elderly if it reduces the likelihood of urinary retention, manages the symptoms of OAB and can be delivered in the office or assisted living facility, or by a homecare nurse.

Critical Discussion

Continued from page 16

body image for countless patients. However, this approach is not always successful due to intolerance of side effects of medications or inability to safely lower bladder storage pressures. In such cases second line therapy is necessary. The focus of this discussion was on the most common options today, including augmentation cystoplasty or intradetrusor injection of onabotulinumtoxinA (onaBoTNA).

Augmentation cystoplasty with ileum, colon or rarely stomach has been the gold standard of management of the intractable hostile neuropathic bladder. Dr. Cain reported that it almost always leads to a reliable and long-lasting increase in bladder capacity, and decrease in storage pressures when properly performed with an appropriate length of intestinal segment sewn to a widely bi-valved bladder. Normal renal function is maintained even in cases of chronic renal failure. The improvement in life expectancy of patients with spina bifida in the era of augmentation has been remarkable with a 20-year survival rate of 92.4% in the largest reported cohort of more than 900 patients at Indiana University. The most common causes of death were nonurological infections and pulmonary issues, and the only 2 deaths of renal failure were related to noncompliance with catheterization or preexisting renal disease.

Unfortunately, in addition to involving a major intra-abdominal operation (often in spina bifida patients with a ventriculoperitoneal shunt for associated hydrocephalus), bladder augmentation is associated with significant life-long risks as noted in 34% of the Indiana series. These risks include bladder calculi (15%), need for re-augmentation (9%) (early in series before modification of initial surgical techniques), bladder perforation (5%), bowel obstruction (3%), and bladder cancer (0.6%). The risk of cancer in the Mayo Clinic experience was 4.6% of augmented bladders (1.5% risk per decade) but it is unclear if this risk was greatly elevated over neuropathic bladders managed with intermittent catheterization without prior surgery. Bladder rupture, another feared potentially lethal complication, has been linked to patient factors such as poor compliance with catheterization regimen or alcohol abuse. Bladder calculi occur in 10% to 50% of bladders following augmentation as a single large or multiple small stones. Data from Indiana have shown that recurrence rates do not differ if stones are extracted intact or endoscopically fragmented. The best way to reduce the risk of occurrence or recurrence is with high volume lavage of up to 240 ml to remove intestinal mucus.

Dr. Lorenzo reiterated that the 10-year risk of death after augmentation is 1.8% and cumulative risk for additional procedures is up to 35% per individual. Since these risks will only increase as our young patients get older, what we are seeing now may only be the tip of the iceberg, particularly in terms of future cumulative incidence of adverse outcomes. Use of onaBoTNA may obviate these potential long-term risks and has been shown to have an exceedingly safe track record in multiple international studies since its introduction 15 years ago. Likewise, it is effective in properly selected patients. Experience from Toronto has shown significant increases in bladder capacity of 27.0% after 1 injection and 37.5% after subsequent injections, and bladder compliance increased 45.2% after 1 and 55.1% after multiple injections. Bladder volume at first detected leakage increased 18.7% and 38.6%, respectively. Studies from the U.S. and UK have indicated onaBoTNA injections to be cost-effective also for neurogenic detrusor overactivity.

A key question that still remains is who most benefits from injection of onaBoTNA and who will see no benefit. Dr. Lorenzo noted that in some cases noncompliant bladders accumulate type III collagen rather than the more elastic type I. Furthermore, it is concerning that injection of onaBoTNA may lead to greater deposition of collagen with more collagen accumulation found in nonresponders. These findings suggest consideration of not just the pre-operative host factors for proper patient selection, but also postoperative biological factors that may be potentially modifiable with agents such as collagenase.

What are the indications for bladder augmentation in 2016? According to Dr. Cain, the primary indications continue to include significant preexisting renal loss, loss of bladder compliance or severe reduction of bladder volume. Secondary indications are failure of medical management, bladder deterioration after an outlet procedure (reported in 28% to 45% of such operations) or failure of treatment with onaBoTNA.

Dr. Cain also presented data from the Pediatric Health Information System® database indicating that the use of onaBoTNA in children increased fivefold in the last 6 years while the rate of bladder augmentation has remained relatively constant during the same period. This finding suggests that injection is unlikely to replace intestine for the management of the hostile neuropathic bladder but offers a less invasive and less morbid approach for less severe cases. onaBoTNA may lose efficacy over time, requiring repeat injections. Controversy exists over diminished effect with more injections due to antibody production against the toxin protein. We use both approaches for the management of the hostile neurogenic bladder. Future research will hopefully better define which treatment is best for given individual patient characteristics. For now, augmentation appears to be best for the bladder with more trabeculation secondary to fibrosis for which onaBoTNA is less likely to improve capacity and compliance.


Take Home Message: Female Urology/Incontinence/ Urodynamics

Benjamin M. Brucker, MD, New York, New York, provided the audience with highlights of the AUA meeting on female urology, incontinence and urodynamics. The abstract numbers are indicated in parentheses.

There were also many excellent studies presented about the treatment of OAB. In a study on improved outcomes with mirabegron add-on treatment, patients who remained incontinent after 5 mg solifenacin run-in were randomized to combination therapy (solifenacin 5 mg + mirabegron 25 mg, increasing to 50 mg), solifenacin 5 mg and solifenacin 10 mg (PD36-01). The end points of this study were health related quality of life measures and treatment satisfaction, and combination therapy outperformed both doses of solifenacin as monotherapy in those domains.

The results of the ROSETTA trial were also presented (PI-LBA01). A group of patients with severe OAB were randomized to sacral neuromodulation and onabotulinumtoxinA (200 U dose). The primary end point at 6 months was a reduction in daily urgency urinary incontinence episodes. OnabotulinumtoxinA outperformed sacral neuromodulation in the primary end point, and it also achieved a higher rate of complete resolution of urgency urinary incontinence (20% vs 4%, respectively, p <0.0001). Adverse outcomes were also assessed. Patients in the onabotulinumtoxinA group had an intermittent catheterization rate of 16% at 2 weeks, 8% at 1 month and just 2% at 6 months. Revision/removal of the sacral neuromodulation device was 3% at 6 months.

Nocturia was another topic on which some exciting work was presented. This common condition has significant quality of life implications and one of the first steps in addressing this condition is understanding what underlying factors contribute to the disease burden. In a study on the link between socioeconomic and dietary factors and nocturia, investigators looked at data from the National Health and Nutrition Examination Survey, and found that family income, as manifested by grocery spending and dietary quality, is a robust predictor of nocturia (MP74-03). The authors call for policy changes that will result in the prevention of this condition by simply providing access to less expensive, higher quality foods.

The other development in the study of nocturia was the presentation of a phase 3 study of a new nasal formulation of low dose desmopressin, SER-120 (MP74-01). The group studied reflects typical urology patients with this com-
plaint, and all patient types (benign prostatic hyperplasia, male, female, OAB etc) were included if they had 2 or more voids per night. The drug outperformed placebo by improving the number of nighttime voids. The trial also showed that the formulation was safe with only 0.76% of patients in the higher dose group (1.5 mcg) and none in the lower dose group (0.75 mcg) having hyponatremia (defined as serum sodium less than 125 mmol/l or less than 130 mmol/l with symptoms). This will be an exciting tool in the nocturia treatment armamentarium.

Pelvic organ prolapse is another prevalent condition that affects many female patients. One group used a 5% sample of Medicare data to look at long-term outcomes of various routes of apical prolapse repair (MP10-04). The patient (“apex only”) prolapse reoperation rates were analyzed based on the route of the index repair (vaginal vs abdominal). Reoperation rates for prolapse at 10 years were 20.7% for the vaginal repair group and 7.9% for the abdominal repair group (p=0.003). The data set has some limitations that the authors acknowledge (ie lack of severity assessment, lack of rationale for specific procedures), but it does provide valuable insights and direction for further work on the durability of repairs.

Resident education is important, as we must balance the need to train a workforce to care for an aging population and contain health care costs. An examination of outcomes of minimally invasive abdominal sacrocolpopexy with resident operative involvement deserves mention (MP10-07). The NSQIP® (National Surgical Quality Improvement Program) database was explored for patients who underwent laparoscopic or robotic sacrocolpopexy for pelvic organ prolapse from 2006 to 2012. Coding for resident participation and level of resident training was used to explore the impact on surgical times and surgical outcomes. Operative participation of a senior resident (post-graduate year [PGY] greater than 4) in minimally invasive sacrocolpopexy resulted in a longer operative time and this was not the case for more junior residents (PGY less than 4). Length of stay and all other 30-day perioperative outcomes were not affected by resident involvement in the surgical case. Thankfully safety and quality were maintained.

One of the urodynamic presentations that should be highlighted describes a novel technique using ultrasound

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**Figure 1.** Overactive bladder CCP. **PE,** physical examination. **PFMT,** pelvic floor muscle training. **MRI,** magnetic resonance imaging. **LE,** lower extremity.
during urodynamics to assess for detrusor wall tension and stress (PD06-12). Ultrasound images were obtained during the urodynamic filling phase, and the authors describe calculating wall tension as vesical pressure x luminal area, wall stress as wall tension/wall area, and strain as the change in inner perimeter/inner diameter at 10% capacity. Traditional vesical pressure during filling remained flat, but wall stress increased linearly and compliance decreased exponentially. The logical next step to validate this technique is to show the clinical importance of these measures.

The negative impact of radiation therapy on artificial urinary sphincter (AUS) outcomes has not been clearly shown. However, now in a multicenter analysis investigators evaluated 56 patients with idiopathic AUS cuff erosion (MP87-09). The erosion-free median surgical survival was 3.15 years without radiation vs 1.00 years with radiation (p=0.0327). These data will be useful in counseling patients about device survival and reoperation rates.

Figure 2. Patient friendly “roadmap” to complement the CCP with a patient friendly format and language

Clinical parameters (leak point pressure and baseline external urinary sphincter electromyography amplitude) also improved after active treatment. If these findings could be reproduced in human birth injury, would electrical stimulation have a place in shortening the duration of postpartum stress urinary incontinence or even in the prevention of vaginal birth trauma related incontinence later in life?

The Female Urology/Incontinence/Urodynamics sessions at the AUA were outstanding. SUFU, the program chairs, abstract reviewers, presenters and AUA staff all need to be thanked for a job well done. Attendees of the 2016 San Diego AUA meeting left satisfied, informed about cutting-edge research and excited for an encore performance next year in Boston.