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Overactive Bladder: Utilization of Third Line Therapies*

Learning Objective: At the conclusion of this continuing medical education activity, the participant will be able to describe each third line therapy recommended for the treatment of overactive bladder and apply the clinical care pathway to their management of overactive bladder.

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***This AUA Update addresses the Core Curriculum topic of Urinary Incontinence and Overactive Bladder, and the American Board of Urology Module on Neurogenic Bladder, Voiding Dysfunction, Female Urology, BPH and Urethral Stricture.**

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INTRODUCTION

Overactive bladder is a symptom complex with 4 major components consisting of urgency, frequency, nocturia and urge incontinence. Patients may experience varied combinations of these symptoms. However, urgency is considered the hallmark of overactive bladder.[1] It is important to note that underactive bladder may present with similar symptoms to overactive bladder, but these are secondary to incomplete emptying and elevated post-void residuals/and or retention. As a result, it is critical to perform a complete history and physical evaluation to rule out potential causes of underactive bladder, including neurological/pelvic injuries, chronic conditions such as AIDS, syphilis and diabetes, neurological disorders and spinal cord injuries/trauma/degeneration, etc.[2]

Treatment algorithms and guidelines have been designed to provide goal-oriented therapy and direction for clinicians in order to optimize patient quality of life and maximize symptom control. The American Urological Association/Society for Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction Guidelines for diagnosis and treatment of OAB in non-neurogenic adults, published in 2012 and amended/revised in 2014 and again in 2019, reflects the most current body of evidence for treatment modalities (https://www.auanet.org/guidelines/overactive-bladder-(oab)-guideline). In 2017, SUFU released the OAB Clinical Care Pathway as an aid to enhance the functionality of guidelines, making it easier to implement.

Use of such algorithms and pathways allows for the optimization of OAB treatment with emphasis on appropriate evaluations while minimizing unnecessary testing. OAB should be managed in a stepwise fashion based on appropriate evaluation of signs/symptoms. This is accomplished by accurate history and physical examination and urinalysis. Use of additional testing such as post-void residual, UDS or cystoscopy is not routinely needed for straightforward OAB. However, for the patient who is considering third line therapy, the question arises as to whether they are suffering from straightforward but refractory OAB vs complicated OAB. Additional testing can be considered when evaluating the patient who has complicated OAB or possibly multiple causes contributing to their lower urinary tract symptoms.

The treatment hierarchy for OAB includes first, second, third and fourth line therapies, and was established based on the balance of risks and benefits, invasiveness of treatment and the duration of adverse effects that could occur as a result of selected therapy. **First line treatment is directed at behavioral modifications including bladder training, delayed/timed/double voiding, pelvic floor muscle training, urge suppression, biofeedback, fluid management, avoidance of bladder irritants, etc.**[3–7] **The addition of pharmacological agents such as beta3-agonists or anticholinergics encompasses the second line therapies for OAB.** These agents can be utilized in conjunction with behavioral modifications to optimize OAB symptom control. It is recommended to proceed with dose adjustments, extended release versions of medications and combination therapy (beta3 and anticholinergic) when the patient experiences inadequate symptom control or adverse effects, including dry mouth, dizziness, constipation, cognitive dysfunction and blurred vision.[8,9]

DEFINITION OF THIRD LINE THERAPIES

Third line therapies may be offered to patients with failed first and second line therapies, or patients who are not candidates for the aforementioned therapies. In patients who are unlikely to comply with the time and effort commitment necessary to achieve optimal effects with behavioral therapies, it may be prudent to advance to second or third line therapies. Those who are unable to tolerate adverse effects of second line therapies (constipation, dry mouth, urinary retention etc, despite dose adjustment) or have other mitigating risk factors (other medications with anticholinergic properties, narrow angle glaucoma, prescribed oral forms of potassium chloride, underlying gastric emptying delay etc) may be transitioned to third line therapies.[10,11] **These therapies include sacral neuromodulation, peripheral tibial nerve stimulation and/or bladder chemodenervation with onabotulinumtoxin.**

PTNS is defined as peripheral stimulation of the tibial nerve located approximately 3 to 5 cm cephalad from the medial malleolus. The effects on bladder storage and emptying reflexes are due to the fact that the posterior tibial nerve contains motor and sensory signals from the L4 to S3 nerve roots. Stimulation of this nerve activates somatic afferent fibers, which send inhibitory signals to the sacral and central pontine micturition center, allowing for bladder activity inhibition and improved storage. PTNS achieves a persistent inhibitory impulse to these nerve roots and thus allows the therapeutic effect to continue once the stimulation is removed.[12,13] This modality is employed typically with 12 weekly 30-minute sessions of stimulation in the office setting. The amplitude of device stimulation is increased until motor and sensory responses of the big toe (motor/flexion) and sole/toes, respectively, occur. The current is then adjusted/increased based on patient comfort with stimulation/sensation. If a patient has improvement of OAB symptoms, additional monthly therapies can be utilized. **PTNS can be considered in those who have not undergone second line therapies with pharmaco-management of OAB given the low risk of adverse effects associated with PTNS in addition to the reversibility of the therapy**.

BTX is derived from the gram-negative rod anaerobic bacteria known as *Clostridium botulinum*, which acts as a potent neurotoxin. **The mechanism of action of BTX occurs through inhibition of pre-synaptic acetylcholine release at the neuromuscular junction, essentially resulting in a flaccid paralysis.**[14] **The recommended effective dose of BTX for OAB is 100 U, which has been shown to have similar efficacy with improved safety profiles compared to higher dosing (up to 300 U).**[15] This can be performed with flexible or rigid cystoscopy and endo-

ABBREVIATIONS: AUA=American Urological Association, BPH=benign prostatic hyperplasia, BTX=onabotulinumtoxin, CCP=clinical care pathway, CIC=clean intermittent catheterization, LUTS=lower urinary tract symptoms, MRI=magnetic resonance imaging, OAB=overactive bladder, PTNS=posterior tibial nerve stimulation, PVR=post-void residual, SNM=sacral neuromodulation, SUFU=Society for Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction, UDS=urodynamics, UTI=urinary tract infection, UUI=urinary urge incontinence

scopic needle with injection of 1 ml BTX at 20 to 30 sites and should be injected beneath the bladder detrusor mucosa into the muscularis layer.[16] A general recommendation for injection patterns includes starting just proximal to the trigone and working laterally from right to left (or vice versa), and then returning to midline and performing another row of injections 0.5 to 1 cm above the last row completed.[17]

SNM (InterStim®) is a U.S. Food and Drug Administration approved treatment modality for refractory OAB, specifically urgency incontinence and urgency-frequency.[18,19] SNM functions as a pacemaker for the bladder, in which electrical impulses are delivered to the S3 sacral nerve root that is responsible for innervation of the autonomic functions of the pelvic nerves as well as striated muscles (levator ani). **Motor responses to S3 stimulation result in "bellows" (contraction of pelvic floor, causing an inward pull of the intergluteal fold and/or anus) and plantar flexion of the great toe.** Sensation of S3 stimulation is felt in the rectum, extending anteriorly to the scrotum in males and the labia in females.[20] The mechanism of action of SNM is not explicitly understood. However, it is proposed that SNM may activate the bladder somatosensory afferent fibers that regulate both the pontine micturition center and the hypogastric sympathetic nerves. Furthermore, recurrent and repetitive stimulation of the S3 nerve by SNM downregulates the bladder's contractile responses and can result in an overall reduction of detrusor muscle overactivity.[21]

ADVANTAGES AND DISADVANTAGES OF PTNS, BTX AND SNM

PTNS. **Overall, PTNS is a well-tolerated, minimally invasive, low risk profile treatment modality for OAB with success of 60% to 80% (as compared to pharmacotherapy and sham PTNS).**[22] Most studies measure outcomes including incontinence, nocturia, frequency and quality of life, and PTNS overall demonstrates improvement in all measured outcomes.[23] Following typical protocols of 12 weekly sessions, PTNS results in symptom control benefits for up to 6 months following discontinuation of therapy,[24,25] and long-term data as described by Yoong et al[26] and Peters et al[27,28] illustrate the maintenance of treatment effects with the continuation of therapy at less frequent intervals (1–2 treatments monthly; median number of yearly treatments 8–9). In addition, studies have demonstrated that compared to SNM and BTX over a 2-year treatment period, PTNS is more cost-effective (including both initial 12-week therapies and maintenance).[29,30] Limitations to treatment with PTNS are often patient driven, eg inability to maintain weekly clinic appointments to sustain therapy for its prescribed duration. In order to optimize durability of therapy, it may be beneficial for patients to participate in a maintenance regimen as described above, which may require more long-term patient commitment to sustain benefits of PTNS therapy. This can often be limiting due to financial, time and resource constraints (table 1).

Overall, the ideal candidate for PTNS is a motivated, well-counseled patient with moderate to severe OAB symptoms. **Contraindications to PTNS include lower extremity edema, proneness to excessive bleeding, presence of pacemakers/implantable defibrillators and pregnancy or planning for pregnancy.**

BTX. **One of the most common adverse effects from BTX is urinary retention or elevated post-void residuals that may require temporary clean intermittent catheterization.** The rates of urinary retention are highly variable in the literature (10%–40%) and are typically dependent on the definition of urinary retention (ie PVR >200 cc, urinary complaints, initiation of CIC). Preoperative PVR >100 cc and increased bladder capacity have been shown to raise the overall risk of urinary retention, and therefore patients should be counseled prior to injection on the need for CIC following the procedure. This adverse outcome may contribute to increased risk of urinary tract infection following BTX injections, and patients should be counseled accordingly (table 2).[31,32]

Antibody-mediated toxin resistance secondary to antibodies to botulinum toxin may be exacerbated by more frequent dosing interval and higher treatment dosing.[33] This resistance has not been established specifically in bladder tissue. However, it could be anecdotally applied to those patients considered

Table 1. PTNS as third line therapy

Study Population	References	Outcomes Summary
Men and women with OAB who underwent 12 weekly 30-min sessions of PTNS	Peters et al[44] (Study of Urgent® PC vs Sham Effectiveness in Treatment of Overactive Bladder Symptoms [SUmiT])	Primary: moderate to markedly improved global response assessment in 54.5% of PTNS pts vs 20.9% of sham group (p <0.001); secondary: statistically significant improvement in global response assessment subsets of urgency, frequency and UUI for PTNS compared to sham; adverse events: bruising in 0.9%, discomfort at needles site in 1.8%, bleeding in 2.7% and tingling in 0.9% of PTNS pts vs none in sham group
Men and women with urinary frequency with or without previous anticholinergic therapy who underwent 12 weekly sessions of PTNS vs 4 mg tolterodine extended release daily	Peters et al[22] (Overactive Bladder Innovative Therapy [OrBIT])	Primary: global response assessment revealed cure or improvement in 79.5% of PTNS pts vs 54.8% of tolterodine group (p=0.01); at 12 wks frequency, UUI, urge severity and nighttime voids improved similarly for both groups; no significant adverse effects were noted in either group

Table 2. BTX as third line therapy

Study Population	References	Outcomes Summary
Women with UUI refractory to 2 first line therapies who received 200 U BTX vs placebo	Brubaker et al[45]	Clinical response on PGI-I—overall 60% of pts had clinical response with duration of 373 days (vs 62 days with placebo, p <0.0001), 43% had PVR >200 cc and 44% had UTI (vs 22% on placebo); elevated PVR and UTI resulted in hold on study
Men and women with >2 daily UUI episodes and >100 gm 24-hr pad wt who received 200 U or 300 U BTX vs placebo	Flynn et al[46]	Significant decrease in pad use at 6 wks in BTX group; no difference in nocturia, frequency, peak flow or detrusor pressures; 26% of pts had PVR >200 cc; no significant differences were observed in UTI between 2 groups
Men and women with detrusor overactivity on UDS with or without UUI who received 200 U BTX vs placebo	Sahai et al[47]	Significant decrease in frequency and UUI in BTX pts at 4 and 12 wks; increased PVR at 4 wks became insignificant by 12 wks

nonresponders to BTX. BTX can be offered in the office setting with flexible or rigid cystoscopy (although patient anatomy, etc, should be considered because it may limit the ability to provide care in the office, such as in patients with any physical constraints not allowing for positioning in stirrups, etc) or under intravenous sedation in the operating room, although this may not be feasible for patients who are poor surgical candidates or at higher risk for complications with the addition of anesthetic.[34]

Overall side effects of the BTX itself are minimal, with systemic absorption/effects being rare, and include generalized weakness, optic changes such as blurred vision and diplopia, and dysphagia.[35] More commonly reported side effects include site injection pain, hematuria and periprocedural urinary tract infections. Currently, there are no specific guideline recommendations for the use of prophylactic antibiotics during BTX injection, which is therefore at the discretion of the physician.[31] Acute urinary retention or elevated post-void residuals may be more commonly seen in males and patients with a history of elevated PVR (>100 ml) and can be managed by temporary indwelling urethral catheter vs intermittent self-catheterization.[17]

SNM. **The success of OAB treatment with SNM has been defined as >50% improvement in daily average episodes of incontinence, number of voids and/or return to normal voiding frequency (<8 voids a day).** Recent literature demonstrates overall higher rates of success with SNM compared to second line therapies with antimuscarinics in all of the previously discussed outcomes, in addition to quality of life, sexual function and depression scores (table 3).[36]

The evolution of SNM surgical techniques and design has proven beneficial in the overall reduction of patient morbidity. For example, there has been a significant size reduction in implantable pulse generators, with devices initially requiring abdominal placement and now allowing for insertion in the upper buttock subcutaneous tissue. In addition, blind techniques for lead placement have now been replaced with fluoroscopic placement based on specific anatomical locations, and ultimately placement is optimized with self-anchoring tined leads.[37,38] Finally, SNM can be performed as a staged procedure in which the lead is placed and connected to a percutaneous lead extension and battery transceiver, allowing for a period of test stimulation (typically 7 days). Everaert et al showed a 2-stage implant had a higher success rate than a single stage and decreased technical failure,[39] while other randomized trials have demonstrated improved outcomes in a staged placement vs percutaneous nerve evaluation.[40,41] For some patients, the downfall of the staged approach is the necessity of 2 anesthetic procedures.[42]

Patients should be counseled on the risks of SNM, including pain at the insertion site (most common), infection (potentially requiring removal of battery, lead or all components), need for surgical revisions if trauma/insult to lead occurs, battery exchange (typical battery life is 3–5 years) and the limitations of magnetic resonance imaging. There are emerging technologies in the SNM realm including rechargeable batteries (estimated lead and battery life of 15 years) and MRI compatibility in 1.5 T machines developed by Axonics Modulation Technologies® and Medtronic (Fridley, Minnesota), with MRI compatible leads allowing use in full-body 1.5 T and 3 T MRI being released for clinical use in Europe in January 2020.[43]

USE OF THE CARE PATHWAY TO GET TO THIRD LINE THERAPY

The management of OAB has been well established and with the emergence of new therapies has resulted in guidelines designed to approach treatment in a stepwise fashion in order to optimize patient satisfaction while minimizing risks and unnecessary testing. It is paramount to ascertain the expectations and goals of the patient when utilizing the OAB care pathway. Improving communication with the physician such that the patient does not feel embarrassed or unwilling to share their concerns and frustrations can facilitate more seamless movement through the care pathway. Initial evaluation should include determination of symptoms and current barriers to quality of life secondary to bladder symptoms. A standardized method for quantifying patient symptoms can best be determined by the use of validated questionnaires such as the Patient Global Impression of Improvement (PGI-I); 8-Item Overactive Bladder Questionnaire (OAB-8); quality of life; Urinary Distress Inventory, Short Form (UDI-6); Incontinence Impact Questionnaire, Short Form (IIQ-7), etc. These questionnaires can also be beneficial in determining patient-perceived progress or improvement in symptoms from visit to visit. An invaluable resource to both patients and physicians is the SUFU OAB CCP (https://sufuorg.com/resources/overactive-bladder-ccp.aspx), which provides educational tools including provider

Table 3. SNM as third line therapy

Study Population	References	Outcomes Summary
Men and women >16 yrs old with medication refractory urgency-frequency who had >50% improvement during test stimulation	Hassouna et al[18]	At 6 mos: improvement in number of voids, vol per void and degree of urgency in SNM pts vs controls (p <0.0001); stimulation was removed at 6 mos and symptoms returned to baseline; sustained efficacy was noted at 12 and 24 mos. At 12 mos: 15% of SNM pts had pain at battery site, 9% had new pain, 8% had lead migration, 6% had infection, 5% had transient sensation of electrical shock and 5% had pain at lead site.
Men and women >16 yrs old with medication refractory UUI who had >50% improvement during test stimulation	Schmidt et al[19]	At 6 mos: SNM pts had reduction in daily incontinence episodes, severity of episodes and pad/diaper replaced daily due to UUI (p <0.0001); 47% of SNM group (16/34 pts) were completely dry and 29% had >50% improvement; efficacy was sustained for 18 mos. Adverse events included generator site pain in 15.8% of pts, lead site pain in 19% and lead migration in 7%; 32% of pts underwent revision without further complication.
Men and women >20 yrs old with medication refractory UUI who had >50% improvement during test stimulation	Weil et al[48]	At 6 mos: observed 90% reduction in leakage episodes, 92% reduction in pad use and 24% decrease in mean leakage severity vs no change in controls; 56% of pts were dry at 6 mos and 32% had treatment failure at 36 mos. Adverse events: 42% of pts had pain at generator site, 21% had lead migration and 18% had leg pain.

flowcharts and patient roadmaps detailing the pathway for treatment of OAB. The SUFU OAB CCP has the PGI-I built into the smartphone app as a mechanism to improve patient outcomes and reduce the risk of patients being stuck with an unsuccessful treatment option.

In addition, adequate patient followup once initiating treatment is necessary to ensure that therapies are well understood and being utilized properly, and questions are answered in a timely fashion with minimal delays in changes of care, especially in patients who may be failing a certain line of therapy and should be offered new options for treatment. Timely followup will also allow the physician to recognize patients who may have more complex bladder dysfunction and not just refractory OAB and employ the appropriate testing modalities that may help better characterize the complex etiologies of OAB (eg cystoscopy, UDS, urine culture). UDS (with or without video) should be utilized in patients who have not responded to first and second line therapies, who may have underlying neurogenic or other bladder dysfunction, in which case certain invasive therapies may be more or less effective.[49]

Refractory OAB is urgency-frequency with or without urinary incontinence remaining bothersome after adequate behavioral and medical therapy for 8 to 12 weeks (medication must be used for a minimum of 4 to 8 weeks). However, this does not include those who fail therapy due to side effects or inability to comply with treatment strategies based on other barriers.

The OAB guidelines and CCP were significantly revised in 2014, most specifically regarding the changing of PTNS from "optional" to "recommended" therapy and BTX from "optional" to "standard" treatment (following U.S. Food and Drug Administration approval for non-neurogenic OAB). Additional changes at that time also included beta3-agonists in the category of medications used in second line treatment. In 2019, the AUA/SUFU introduced several new updates to the OAB guidelines, one of which allowed for progression of patients to third line therapies, specifically PTNS, earlier in the algorithm or in combination with behavioral therapy and/or medications. This was specifically noted due the limited invasiveness of PTNS therapy and minimal adverse effect profile.

Ultimately, the CCP should be used in a manner in which each individual patient case is considered, and often combinations of therapies (ie behavioral with PTNS) can be used in order to maximize patient symptom improvement. **While the guidelines imply that patients should be offered each line of therapy before advancing to the next level, they do not dictate that the patient must go through each line of therapy prior to advancing to additional lines of therapy in the algorithm. It is necessary to consider the patient, potential adverse outcomes/side effects, barriers to treatment, compliance etc when determining which line of therapy is most appropriate.** This may be more commonly seen with early adoption of PTNS, given that it is minimally invasive with a low risk profile.

There are particular patient populations that need to be considered when utilizing the CCP for OAB, including the elderly/frail, patients with underlying neurogenic dysfunction and males with lower urinary tract symptoms associated with OAB. Specifically, the guidelines and care pathway were established based on non-neurogenic OAB, and therefore it is necessary to rule out neurogenic bladder dysfunction to ensure appropriate use of therapies. The elderly or frail patient population (with impaired cognition, strength, physical activity, balance, etc) has a higher risk of adverse effects, a lower therapeutic dose index and a greater likelihood of polypharmacy, and often cannot tolerate second line therapies in the CCP.[50] They be more appropriate for combination of first line behavioral modifications in conjunction with less invasive third line therapy such as PTNS.

Males with LUTS associated with OAB can often be a difficult subgroup of patients presenting with multiple potential etiologies of bladder dysfunction and symptomology. It can be difficult to determine if their symptoms are secondary to outlet obstruction (ie benign prostatic hyperplasia) or an underlying component of OAB. These patients are often initiated on BPH

medications such as alpha blockers and/or 5alpha-reductase inhibitors in order to address the obstructive voiding symptoms. However, it must be understood that the mechanism of action of these medications will solely address the outlet and will not impact any underlying OAB pathophysiology. **Because BPH and OAB components can coexist, it is recommended to start patients on therapies that will address both components of bladder dysfunction, eg an alpha blocker in conjunction with antimuscarinics. The NEPTUNE trial demonstrated statistically significant improvement in urgency scores for a combination of 0.4 mg tamsulosin/6mg solifenacin vs tamsulosin alone or placebo.**[51] The risk of urinary retention or elevated post-void residuals often deters physicians from initiating antimuscarinic therapy in males with BPH. However, this decision is often based on anecdotal evidence or supposed risks. Indeed, a randomized blinded clinical trial assessing the use of anticholinergics in men with bladder outlet obstruction revealed the rate of retention was no different in men on anticholinergics vs placebo.[52] However, judicious monitoring of PVR is not unreasonable, and the risk of retention may impact a provider's choice of third line therapy.

Furthermore, if bothersome symptoms persist, additional diagnostic testing such as cystoscopy and UDS can be considered if the etiology of male LUTS is unclear. Luckily, the obstructive component often improves with therapy and may not be the primary etiology of bothersome symptoms. Once the provider has confirmed that an obstructive component is not contributing to a patient's LUTS, then third line therapies can be considered.

CONCLUSION

The AUA/SUFU guidelines for treatment of non-neurogenic OAB combined with the SUFU OAB Clinical Care Pathway may be used to treat a symptom complex that can often be difficult to manage. It is essential to establish patient goals and expectations of treatment and outcomes early in the process, and to maintain close followup throughout the process in order to ensure efficacy and overall patient satisfaction. The provider should be able to delineate the difference in patients with LUTS due to refractory yet uncomplicated OAB vs patients with complicated OAB who may have other causes contributing to their LUTS, and then employ testing as needed to further characterize these patients. Male patients with persistent LUTS can be particularly challenging since it can be difficult to determine if LUTS are due to persistent obstruction vs OAB. However, once an OAB component is confirmed, the urologist has multiple third line therapy options to choose from in this population, some of which can be tailored to specific populations (eg SNM is preferred over BTX for the male with OAB who has concomitant emptying problems).

DID YOU KNOW?

- Third line OAB therapies include sacral neuromodulation, peripheral tibial nerve stimulation and/or bladder chemodenervation with onabotulinumtoxin.
- The AUA OAB guidelines imply that not all patients must go through each line of therapy prior to advancing to additional lines of therapy in the algorithm if certain parameters exist.
- The SUFU OAB Clinical Care Pathway provides educational tools including provider flowcharts and patient roadmaps detailing the pathway for treatment of OAB and should be applied to management strategies.

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Study Questions Volume 40 Lesson 10

1. A 65-year-old woman with a history of atrial fibrillation on rivaroxaban (Xarelto®) returns to the clinic with refractory OAB that is nonresponsive to an appropriate course of anticholinergics and beta3-agonist. The next step is to
   a. prescribe a different anticholinergic
   b. perform urodynamics
   c. initiate a 12-week course of PTNS
   d. recommend 100 U intravesical BTX

2. An 80-year-old woman with poorly controlled hypertension, early-onset dementia and symptoms of urgency, frequency and urge incontinence wishes to pursue treatment of her symptoms. She has previously failed behavioral modifications. The next step is to
   a. start 5 mg solifenacin daily
   b. recommend CIC 3 times daily
   c. perform cystoscopy and urodynamics
   d. initiate a 12-week course of PTNS

3. A 55-year-old man with refractory OAB undergoes injection of 100 U intravesical BTX and returns to the clinic 2 weeks post-procedure with worsening symptoms. Urinalysis is performed and is negative. The next step is to
   a. obtain post-void residual
   b. begin intermittent catheterization
   c. place an indwelling urethral catheter
   d. repeat injection of 100 U BTX

4. A 65-year-old woman is undergoing placement of a sacral neuromodulator in a staged approach. The expected motor response for S3 nerve placement is
   a. inward pull of the anus only
   b. plantar flexion of the great toe only
   c. inward pull of the anus and plantar flexion of the great toe
   d. inward pull of the anus and calf rotation

5. A 70-year-old man with BPH and OAB is currently on dual therapy with finasteride and tamsulosin with improvement in weak stream, straining and incomplete emptying. He continues to complain of urgency and urge urinary incontinence despite 6 weeks of trospium. The next step is
   a. continue trospium for 6 more weeks
   b. cystoscopy
   c. 2-stage SNM
   d. transurethral resection of the prostate

ERRATUM

Intravesical BCG Therapy for Bladder Cancer

Volume 40, Lesson 2, Page 12: In this study patients with Ta–T1 tumors without concurrent CIS had an estimated probability of being recurrence free at 5 years of 17% for patients receiving doxorubicin and 37% for patients receiving BCG ($p = 0.015$).