Urinary Incontinence

Botulinum Toxin in Urogynecology
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Patient selection: patients refractory to other treatment candidates for botulinum toxin; assessment of refractoriness — check bladder diary on medication; assess urine for inflammation, infection, or crystals; perform urodynamic testing; consider other treatable causes (eg, prolapse, obstruction, pelvic floor weakness)

Medications: compliance with oral therapies often poor; if antimuscarinics fail, add imipramine, which has additive effects with antimuscarinics; side effects (dry mouth and constipation) same as those for antimuscarinics; α-adrenergic activity of imipramine may improve mixed incontinence; small risk for cardiotoxicity; 12.5 to 25 mg safe dose in elderly patients

Botulinum toxin: effective for treatment of patients with spinal cord injury or detrusor-sphincter dyssynergia; inject into internal sphincter cystoscopically or periurethrally, as with periurethral bulking agents; may use electromyography (EMG) or needle EMG; use 100 to 200 units in divided doses at 3, 6, 9, and 12 o’clock, or use spinal needle to inject periurethrally at 2 and 10 o’clock; optimum number of sites and doses unknown; other indications — commonly used for refractory overactive bladder (OAB); to guide dosing, assess whether patient has 1) pure neurogenic detrusor overactivity, 2) complex lower urinary tract dysfunction with detrusor dyssynergia and incomplete emptying, or 3) nonneurogenic OAB (ie, idiopathic or refractory OAB); in patients with nonneurogenic OAB, distinguish among 1) severe lower urinary tract dysfunction, 2) minor detrusor overactivity with weak pelvic floor (may benefit from biofeedback and Kegel exercises), or 3) detrusor hyperactivity with impaired contractility characterized by OAB, retention, uninhibited contractions on urodynamic testing, and large postvoid residual (PVR)

Mechanism of action: toxin binds to receptors of cholinergic nerves and cleaves synaptosomal-associated protein 25, preventing export of acetylcholine to neuromuscular junction

Injection technique: anesthesia — instill cold 1% lidocaine intravesically and use 2% lidocaine jelly to numb urethra; wait 15 min to obtain good anesthetic effect; equipment — use rigid cystoscope with built-in collagen needle, or flexible scope with flexible needle; dose — inject 100 to 200 units in 10 to 20 sites; patients have mild to moderate pain during injection; may use ≤300 units; typically dilute 100 units per 10 mL, but concentrations reported in literature vary; results excellent regardless of technique; site of injection — inject into posterior and lateral walls; avoid dome of bladder to prevent intraperitoneal injection; no increased risk or improved efficacy demonstrated with trigonal injection, but avoiding trigone may prevent vesicoureteral reflux and pain; not clear whether to raise mucosal bleb or inject detrusor, but probably unimportant (toxin diffuses into muscle)

Results: incontinent patients with SCI — trigone injected; ≥90% of patients completely continent within 6 wk; urodynamic testing showed improved reflex volume (volume at first uninhibited contraction), increased capacity, and decreased voiding pressure; results with 200- and 300-unit doses similar; both doses superior to placebo; improvements in subjective and objective outcomes durable at 24 wk; patients with idiopathic detrusor overactivity but no chronic pelvic pain — treatment with 100 units in 30 injections produced 88% success lasting ≥6 mo; success rates low in patients with poorly compliant bladders; 4% required temporary intervention for retention; patients with idiopathic detrusor overactivity — injections increased bladder capacity, reflex volume, first desire to void, and caused mild but acceptable increase in residual volume

Summary of studies: doses range from 100 to 300 units; efficacy similar in most studies; frequency decreases by 40%, urgency improves by 66%, and urge incontinence (UI) improves by ≥80%; some patients require intermittent catherization, but residual urine may represent success for these patients; frequency cannot improve beyond normal level of 6 to 8 voids per day; in patients with idiopathic detrusor overactivity, frequency decreased by >30%, urgency by 71%, and UI by 60% to 90%; urodynamic testing showed increased capacity; treatment equally effective for idiopathic and neurogenic causes of detrusor overactivity

Contraindications: include allergy to product, pregnancy, breastfeeding, and neuromuscular diseases; use caution with agents that can potentiate neuromuscular weakness (eg, amino-glycosides, clindamycin, magnesium salts, quinidine, and chloroquine)

Pelvic pain: includes dyspareunia, pain with defecation, pain with menstruation, vaginal pain, and constipation; muscle tension probably plays role; treatment — botulinum toxin paralyzes and relaxes pelvic muscles and allows rest and healing; for some indications, pain, dyspareunia, dysmenorrhea reduced, and intercourse improved, but many studies uncontrolled; interstitial cystitis (IC) — effect of botulinum toxin on

Educational Objectives
The goals of this program are to improve diagnosis and treatment of urinary incontinence and other urologic and pelvic pain disorders. After hearing and assimilating this program, the clinician will be better able to:

1. Incorporate the use of botulinum toxin into urologic practice.
2. Discuss experimental use of vanilloids for urologic disorders.
3. Identify patients who are candidates for sacral nerve stimulation (SNS) and combine SNS with other urologic treatments.
4. Triage patients with urinary tract disorders based on a careful history, physical examination, urinalysis, and measurement of postvoid residual.
5. Discriminate among common causes of incontinence using historical factors, validated instruments, uroflowmetry, and urodynamic testing.

Faculty Disclosure
In adherence to ACCME Standards for Commercial Support, Audio-Digest requires all faculty and members of the planning committee to disclose relevant financial relationships within the past 12 months that might create any personal conflicts of interest. Any identified conflicts were resolved to ensure that this educational activity promotes quality in health care and not a proprietary business or commercial interest. For this program, Drs. Comiter and Badlani and the planning committee reported nothing to disclose. In their lectures, Drs. Comiter and Badlani present information that is related to off-label or investigational use of a therapy, product, or device.
other neurotransmitters (eg, glutamate, substance P, adenosine triphosphate, and calcitonin gene-related peptide) may help reduce pain; in small uncontrolled study, >66% of patients dem-onstrated subjective improvement in symptom scores, problem indices, frequency, nocturia, pain, and urodynamic parameters; in 2-yr trial conducted in patients with IC, improvements in pain, frequency, nocturia, cystometric capacity, and voiding pressure observed at 2 yr

Conclusions: good alternative for adults with debilitating chronic urologic conditions; side effect profile low, duration of action predictable (6 to 12 mo); use concomitantly with fluid and caffeine restriction, pelvic floor exercises, medications, and neuromodulation

Neuromodulation

Dr. Comiter

Definition: activity in one neural pathway modulates preexisting activity in another through synaptic interaction; stimulation of one nerve allows other neural functions to normalize; biologic neuromodulators include vanilloids (eg, capsaicin and resiniferatoxin [RTX]); electrical neuromodulators use stimulation of sacral, peripheral, posterior tibial, and pudendal nerves

Vanilloids: remain investigational; intravesical capsaicin — excites, then desensitizes; treats triggers of detrusor overactivity by desensitizing C-fibers, leading to inhibition of reflex bladder overactivity; side effects include acute pain and burning; intravesical RTX — more potent but less painful than capsaicin; results — in neurogenic patients, capsaicin produces >50% improvement in UI within 1 mo, compared with placebo; RTX similarly effective and longer lasting (>3 mo)

Sacral nerve stimulation (SNS): pelvic floor dysfunction (PFD) can result in voiding dysfunction; 60% of patients with PFD do not improve adequately with behavioral management or pharmacotherapy; mechanism of action — probably more afferent than efferent; stimulation of afferent nerve to bladder causes modulation of pelvic and pudendal nerves, which stimulates and modulates voiding reflex (quiets motor transmission to bladder, blocking involuntary reflex voiding); low-stimulation current applied to A-delta fiber (myelinated, light-touch, sensory fiber) of sacral root reflexively excites central inhibitory pathways and blocks C-fiber-mediated urge and pain; SNS treats rather than causes retention; messages from brain initiating volitional bladder contractions override SNS

Retention: speaker defines as inability to store due to lower urinary tract symptoms with detrusor underactivity; patients with nonobstructive retention have overinhibition of micturition reflex; may have high residuals and incomplete voiding instead of frank retention; sometimes related to spasticity of pelvic floor; sphincter activity generates afferent input to sacral cord that inhibits bladder evacuation; SNS turns inhibitory process off and promotes bladder evacuation

Placement: patient can try device using temporary lead in peripheral nerve; SNS may also improve fecal incontinence; place electrode through third sacral neural foramen, just beyond anterior bony plate; place pulse generator if trial effective; quadripolar lead — may improve efficacy; minimally invasive lead that reduces lead migration and results in fewer false positives and false negatives; unlike unipolar lead, no need to remove before placing pulse generator

Results: with unipolar lead, >30% of patients proceed to pulse generator, of whom 75% successfully treated, resulting in overall success rate of 22%; however, with staged test using quadripolar lead, 66% of patients have favorable test period and 88% have success with pulse generator at 3 yr, resulting in 50% overall success rate; SNS works over long periods; frequency, urgency, and voided volume improve over time; 33% of patients have 90% improvement; 75% satisfied with 50% improvement; SNS decreases costs for office visits and drugs

Prognostic factors: success rates higher in patients <55 yr of age and in those treated earlier in course of disorder (between 4 and 6 yr); SNS can improve refractory nonobstructive UI after sling surgery; success rates higher in patients with sensory and motor responses upon test stimulation than in those with only sensory response; keep patient awake and talking during placement; patients with normal EMG or some control of pelvic floor may obtain better results; nonobstructive retention observed in women with Fowler syndrome (retention with painful intermittent catheterization required, polycystic ovaries, and pathogenic “whale sounds” on needle EMG); SNS produces 75% to 80% success (defined as halving of PVR); higher infection rates observed, probably due to intermittent catheterization during and after test; storage symptoms (frequency, urgency, and UI) associated with detrusor overactivity with retention, inability to empty, pelvic floor spasm, sensory urgency, and pelvic pain respond to SNS

Posterior tibial nerve stimulation (PTNS): nerve — peripheral mixed sensory and motor nerve originates from L4 to S3; contributes to sensory and motor control of bladder and pelvic floor; stimulation — depolarizes somatic sacral and lumbar afferents, inhibiting preganglionic bladder fibers through sacral cord; few published data exist (insufficient to recommend as initial treatment); 66% to 75% of patients satisfied with continuous PTNS sessions; summary — mode of action probably similar to SNS; data insufficient to recommend PTNS as first-line treatment; more expensive than anticholinergics; 33% to 75% of patients with fecal incontinence improve in short term; patients likely to require maintenance sessions; long-term cure rate and prognostic factors unknown

Pudendal nerve stimulation (PNS): peripheral nerve derived primarily from S2 and S3; entrapment of pudendal nerve usually accompanied by voiding dysfunction and OAB; study results — patients prefer PNS to SNS (less uncomfortable, slightly greater efficacy); cystometry data demonstrate doubling of first desire to void, increased cystometric capacity, and improved volume at first uninhibited contraction; however, delivery system suboptimal, and long-term data unimpressive

Conclusions: use neuromodulation for pharmacologic and surgical failures; success rates high, suggesting possible use as initial treatment

Work-up of Patient with Incontinence

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Assessment: consider how much symptoms bother patient
Frequency: ask about time of occurrence (day or night), volume, and pain; refer patient with daytime small-volume frequency who sleeps through night; if symptomatic at night, consider volume-dependent nocturia related to peripheral pooling of fluid; recent onset of small-volume frequency and dysuria suggests urinary tract infection (UTI); if constant large-volume frequency, suspect renal cause, or drug associated with poor urinary concentration (eg, lithium)

Urgency: ask whether losing urine involuntarily; urgency with fear of leaking equally bothersome to patients as actual wetting
Incontinence: quantify amount of urine lost; postvoid dribbling in men — related to method of voiding rather than prostatic enlargement or outlet; Valsalva maneuver during voiding leads to urine entrapment above membranous urethra; postvoid dribbling in women — causes include hovering over public toilet, and surgical suspension procedure that alters angle of urethra (allows urine to pool in vagina); historically, patient unaware of leakage and describes leakage as occurring after voiding; treat by reshaping habits rather than with medication; leaking with change of position — can occur with OAB or incompetent bladder opening, as in women with funneled bladder neck;
urine entering urethra with change of position can trigger contraction; upon arising in morning, patient may perform Valsalva, allowing urine to enter urethra and trigger contraction

Pain: pain with voiding usually has bladder or urinary cause; pain relieved by voiding suggests IC; pelvic pain sometimes related to guarding in pelvic floor musculature; urethral or vaginal pain associated with IC

**Physical examination:** in women, observe descent or hypermobility of urethra; examine entire pelvic floor, using rectal examination to assess pelvic floor muscles; in men and women, assess sensation and point tenderness; use findings to begin teaching pelvic floor relaxation techniques; in women with recurrent UTI, consider urethral diverticulum; place single blade of speculum against anterior or posterior wall of vagina to assess apposition; Wapartment; success of midurethral sling procedure for stress urinary incontinence (SUI) depends on urethral hypermobility

**Voiding dysfunction:** in women, less recognized than OAB and SUI: 25% of women in tertiary practice present with dysfunctional voiding; in men, etiologies include obstruction, OAB, or both; prostate sometimes blamed for bladder or pelvic floor symptoms; **assessment**—use validated symptom questionnaires; voiding diary helps patients learn their behaviors and allows post-treatment comparison; pad count can estimate leakage; ask patient to record morning voided volume; use data to estimate functional capacity; patients with small capacity may respond better to behavioral training after treatment with anticholinergic

**Management:** in primary care setting, use history, examination, urination, and PVR to make presumptive diagnosis; identify complex cases and refer; treat first with lifestyle intervention and pelvic floor training; off-label pseudophedrine and imipramine useful; uroflowmetry patterns with EMG and audio or visual signal used to train adults or children with pelvic floor overactivity

**Urodynamic studies:** multichannel study with fluoroscopy may intimidate patient and produce abnormal pattern; correlate with initial uroflowmetry to determine whether findings representative

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**Suggested Reading**

URINARY INCONTINENCE

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1. Botulinum toxin can be used in the treatment of which of the following?
   (A) Detrusor-sphincter dyssynergia  (C) Interstitial cystitis
   (B) Refractory overactive bladder  (D) All the above **

2. The mechanism of action of botulinum toxin involves primarily the _______ receptors.
   (A) Cholinergic  (C) \( \alpha \)-adrenergic
   (B) Muscarinic  (D) \( \gamma \)-aminobutyric acid

3. Studies of botulinum toxin indicate it may improve which of the following urinary symptoms?
   (A) Frequency  (B) Urgency  (C) Incontinence  (D) All the above **

4. Botulinum toxin is relatively contraindicated with all the following medications except:
   (A) Imipramine  (B) Aminoglycosides  (C) Clindamycin  (D) Quinidine

5. Of the vanilloids being used investigationally for treatment of urinary incontinence, _______ is more potent but less painful than _______.
   (A) Capsaicin; resinferatoxin  (B) Resinferatoxin; capsaicin **

6. Patients with nonobstructive urinary retention have overinhibition of the micturition reflex, which is often related to spasticity of the pelvic floor.
   (A) True **  (B) False

7. Identify the incorrect statement about sacral nerve stimulation for urinary incontinence.
   (A) Success rates higher in patients <55 yr of age
   (B) For best results, treatment should start earlier in the course of the disorder
   (C) Not effective after sling surgery **
   (D) Sensory and motor responses on test stimulation more prognostic of successful treatment than sensory response alone

8. Pain relieved by voiding suggests a diagnosis of:
   (A) Urinary tract infection  (B) Urethral diverticulum  (C) Interstitial cystitis  (D) Pelvic muscle spasticity

9. Which of the following methods is best for estimation of functional bladder capacity?
   (A) Pad count  (B) Morning voided volume  (C) Voids diary  (D) Validated symptom questionnaire

10. When possible, initial treatment for urinary incontinence should focus on lifestyle intervention and pelvic floor training.
    (A) True **  (B) False

Answers to Audio-Digest Urology Volume 35, Issue 14: 1-B, 2-A, 3-B, 4-D, 5-B, 6-D, 7-D, 8-D, 9-A, 10-B