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Neuromodulation Techniques for the Treatment of the Overactive Bladder

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Voiding dysfunction including urge incontinence, frequency/urgency syndromes, and chronic urinary retention is a common phenomenon in men and women that result from a variety of conditions ranging from local genitourinary factors to widespread neurologic disease. Although the ability to diagnose this condition has improved over the last decade with more precise definitions and better diagnostic equipment, treatment options and clinical outcomes have been less than satisfactory due to poor understanding of the pathophysiology of this challenging clinical problem. In some cases there is a clear etiologic factor underlying the patient's symptoms like frequency associated with detrusor hyperreflexia due to stroke or multiple sclerosis or incomplete bladder emptying due to outlet obstruction in benign prostatic hypertrophy. Unfortunately, the majority of patients who present with voiding dysfunction symptoms have no obvious or treatable source of their symptoms and are confined to treatment primarily focused on symptomatic improvement. Current treatment options are associated with poor cure rates and significant associated adverse effects. This is particularly important considering the widespread scope of this problem, especially among the aging population of this country.

Urge incontinence and frequency/urgency symptoms have recently been classified as subsets of Overactive Bladder (OAB) Syndrome by the International Continence Society. OAB is defined as "urgency, with or without urge incontinence, usually with frequency and nocturia in the absence of local or metabolic factors explaining these symptoms." OAB most probably represents a spectrum of presenting symptoms that include enuresis and pelvic pain. Recently, it has been hypothesized that interstitial cystitis may be a pain variant of OAB. Further research regarding the etiologic pathways of interstitial cystitis is required. Using the criteria established by the ICS, a recent study estimated that 16.5% of the adult population

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in the United States, or 33 million people, suffer from this condition, although not all will require treatment.[1] This is most probably an underestimation as many patients are reluctant to discuss these symptoms with their physician and many physicians do not include a detailed assessment of these symptoms during routine evaluation. It is expected that the scope of this problem will increase with growing patient awareness, increasing physician education, and the aging population. Current treatment options include pharmacotherapy, dietary modification, behavioral techniques, local treatments, and surgery (Table 1). These treatments are associated with cure rates ranging from 30–90% but depend on strict patient compliance, which may be limited by significant side effects and complications. Adverse effects are especially important considerations in the geriatric population as polypharmacotherapy is common and procedures are associated with increased complication rates.

The exact prevalence of urinary retention is unknown but has been predicted to be as high as 25% in women over age 65, 14% in women under age 65, and in 17% of patients overall.[2] Various etiologic factors including neurologic dysfunction, pharmacotherapy, medical disorders, overdistention injury, and psychogenic causes have been implicated, but specific determination is often difficult in every patient. Patients with obstructive voiding dysfunction due to pelvic mass, previous incontinence surgery, or urethral stricture are best treated with surgical correction of the obstruction. Unfortunately, most patients have nonobstructive retention, which carries a poor prognosis with conventional treatments that include pharmacotherapy, catheterization, and surgery (Table

TABLE 1. Current Treatment Options for Voiding Dysfunction

Overactive Bladder Syndrome	Nonobstructive Urinary Retention
Pharmacotherapy	Pharmacotherapy
Anticholinergics	Cholinergics
Antispasmodics	Alpha-blockers
Antimuscarinics	Smooth muscle relaxants
Tricyclic antidepressants	Antibiotics
Antibiotics	Catheterization
Diet modification	Intermittant
Caffeine reduction	Suprapubic
Fluid restriction	Chronic
Behavioral techniques	Behavioral techniques
Bladder retraining	Double voiding
Biofeedback	Suprapubic pressure
Pelvic muscle exercises	Local Treatment
Local Treatment	Urethral dilation
Urethral dilation	Surgery
Hydrodistention	Sphincterotomy
Bladder instillation	Urinary diversion
Surgery	Bladder augmentation
Bladder augmentation	Continent pouch formation
Bladder denervation	Neuromodulation
Urinary diversion	Percutaneous SANS
Continent pouch formation	Interstim sacral nerve
Neuromodulation	Stimulation
Percutaneous SANS	
Interstim sacral nerve	
Stimulation	

SANS = Stoller Afferent Nerve Stimulator.

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1). These poor outcomes are primarily due to poor understanding of urinary retention in women, compounded by the fact that continued retention could often lead to progressively worsening baseline function.

Pelvic pain that includes interstitial cystitis continues to be one of the most challenging and frustrating conditions faced by the practicing clinician. Chronic pelvic pain is most often multifactorial and can result in progressive deterioration in a woman's quality of life due to associated mental stresses and deleterious effects on psychosocial function. Many women seek care from multiple providers over a long time period without adequate diagnosis or treatment of their condition. Some undergo unnecessary surgery without improvement in their pain. There is growing consensus that the nervous system may play an important role in the pathophysiology of pelvic pain syndromes. Nerve-related techniques, like uterosacral nerve ablation and presacral neurectomy, are gaining popularity as conservative procedures performed previous to resorting to hysterectomy. Recently, neuromodulation has been described for treatment of pelvic pain syndromes including interstitial cystitis.

Due to unsatisfactory cure rates and significant associated adverse effects of conventional therapies, there has been growing interest in neuromodulation techniques for the treatment of these challenging conditions. Increased awareness of nervous system involvement in the etiology of various urogenital conditions including OAB, urinary retention, and pelvic pain has further encouraged research and development of neuromodulation techniques for management of difficult patients refractory to traditional treatment protocols. The field is still in its infancy with the first Food and Drug Administration approved device introduced only within the last decade, but initial results are encouraging and offer many patients new hope. This article summarizes the authors' current understanding of neuromodulation, describes currently available techniques, provides a suggested treatment algorithm, and discusses future developments in this exciting new field.

Principles of Neuromodulation

Although a comprehensive discussion of the anatomy and pathophysiology of micturition is beyond the scope of this article, a basic review is necessary to understand the underlying principles of neuromodulation. The bladder and pelvic floor receive the major part of their innervation via the pudendal nerve with 70% contribution from the S3 nerve root and the remaining 30% from S2 and possibly S4. Sacral parasympathetic preganglionic fibers in the pelvic nerve provide the major excitatory input to the bladder while sympathetic pathways originating in the thoracolumber segments of the spinal cord provide balancing inhibition (Fig. 1). Afferent pathways, composed of small, myelinated A-fibers and unmyelinated C-fibers, transmit signals from mechanoreceptors, pelvic visceral organs, and somatic pathways, important for voluntary control of the micturition reflex. Bladder hyperactivity is believed to be mediated by the loss of voluntary control of voiding and the appearance of primitive voiding reflex circuitry, probably due to the formation of new reflex circuits mediated by C-fiber afferents. Animal studies have demonstrated that somatic afferent input to the sacral spinal cord segments can modulate the bladder and guarding reflexes involved in normal voiding and storage.[3] It is unclear whether the effects of neuromodulation are localized to the spinal cord-bladder loop or involve higher nerve centers. Recent data suggest afferent pathways affected by neuromodulation may be mediated via the spino-bulbo-spinal pathways to the pontine micturition center.[4] Pudendal afferent input to the sacral spinal segments can turn off supraspinally mediated hyperactive voiding, blocking the ascending system. Pudendal afferent input can also turn on voiding reflexes by turning off the

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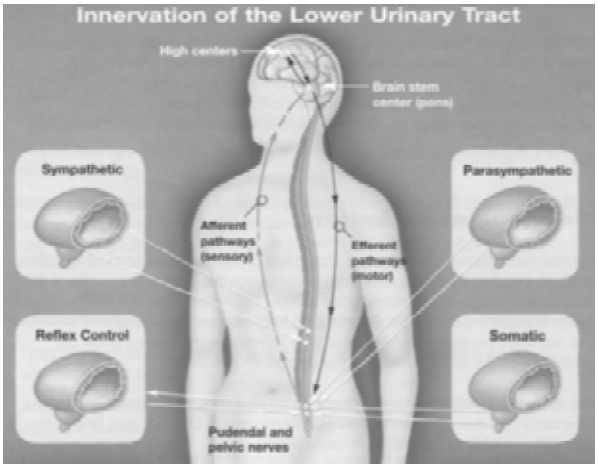

FIG. 1. Diagrammatic representation of spinal cord control of normal bladder storage and emptying.

guarding pathways. Neuromodulation inhibits afferent evoked excitatory reflexes via suppression of interneuronal mechanisms but does not have a prominent inhibitory effect on voluntary voiding that is controlled by direct supraspinal excitatory input by the pelvic ganglion neurons. Despite recent understanding of the possible mechanism of sacral nerve stimulation, electrical stimulation has been used for several decades in the treatment of pelvic floor dysfunction.

Neuromodulation of the pelvic floor for the treatment of incontinence dates back to the 1960s when Caldwell reported the use of electrical stimulation by implanted electrodes to control stress urinary incontinence. Functional electrical stimulation using intravaginal stimulators has been shown to be effective in the treatment of voiding dysfunction in various studies. The current principles and evolving techniques of neuromodulation are based on this historical data and work performed by Drs. Schmidt and Tanagho in the early 1980s.[5] Since that time, great strides have been made in the currently available techniques for sacral nerve stimulation.

Stoller Afferent Nerve Stimulator Peripheral Sacral Nerve Stimulation

The Stoller Afferent Nerve Stimulator (SANS) is a minimally invasive, cost-effective neuromodulation technique approved by the Food and Drug Administration in 1999. The technique uses a monopolar generator to deliver a pulse signal to the posterior tibial nerve via an acupuncture needle placed slightly above the ankle. This area, long recognized as the "bladder center" (Spleen 6) by ancient Chinese acupuncturists, has projections to the S3 sacral segment, creating a feedback loop that neuromodulates bladder innervation. The SANS technique requires no special training or complex equipment.

TECHNIQUE

Peripheral percutaneous neuromodulation is performed in the office without local anesthesia with the patient sitting in the "frog-leg" position. A 34-gauge stainless steel acupuncture needle is placed through the skin three-fingers breadth cephalad to the medial malleolus and advanced approximately 4 cm, posterior to the tibia, at a 30-degree angle toward the ankle. A grounding pad is placed on the heel and the needle connected to a 9-V alternating current monopolar generator, the SANS device. (Fig. 2) Stimulation is selected within a range of 0.5 to 10 mA with a fixed pulse width of 200 μs and a frequency of 20 Hz. Proper stimulation is confirmed by flexion of the great toe or fanning out of digits 2 to 5. Voltage is then decreased until the toe response is relieved

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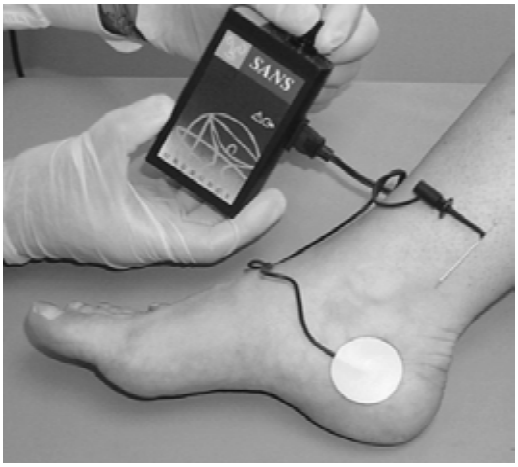

FIG. 2. Stoller Afferent Nerve Stimulator peripheral sacral nerve stimulation performed via acupuncture on the lower leg.

to prevent cramping in the foot. At this level, most patients are just minimally uncomfortable with a "tingling" sensation. Either leg can be used for the stimulation. Many patients report an accommodation response or significant decrease in the stimulation felt after 3 to 5 minutes without adjustment of the voltage setting. Patients initially undergo 12 weekly stimulation treatments, with each session lasting 30 minutes. Those who are found to improve after 12 weeks continue to receive regular treatments according to a tapering protocol.

Following this period, further therapy is individualized, although most responders undergo a slow taper with monthly or biweekly sessions or wait for recurrence of symptoms.

COMPLICATIONS

Complications associated with the SANS peripheral neuromodulation are rare and no significant or permanent adverse effects have been reported to date. Isolated reports of a small self-limited hematoma at the puncture site and residual transient sensation radiating in the leg immediately after the procedure have been noted. Its high safety factor, ease of use, and office-based convenience make it an ideal initial neuromodulation procedure for treatment of OAB, voiding dysfunction, and pelvic pain.

RESULTS

Given the recent introduction of this technique, there is little data regarding the long-term efficacy of peripheral neuromodulation in the treatment of voiding dysfunction. In a recent multicenter study, 53 patients with OAB refractory to traditional therapy received weekly percutaneous electrical stimulations. Urodynamic studies, detailed voiding diaries, quality-of-life surveys, and incontinence impact questionnaires were completed before, during, and after the study. Of the 53 patients, 47 (89%) completed the 12-week study. A total of 71% of patients were classified as treatment successes by the investigators and were started on long-term treatment. On average, patients noticed a 25% reduction in mean daytime and 21% reduction in mean nighttime voiding frequencies ($P < 0.5$). Urge incontinence was reduced by an average of 35% ($P < 0.5$). Statistically significant improvements were noted in selective pain and quality-of-life indexes. No significant adverse events related to treatment were noted in any patients.[6]

In a separate study, Klingler et al[7] reported the Austrian experience with SANS in 15 patients with urgency-frequency syndrome and/or pelvic pain. All patients were assessed with a visual analog scale and urodynamic testing before and after treatment. At a mean follow-up of 10.9 months, reduction in pain was achieved in all patients with a decrease in the Visual Analog Scale from a mean of 7.6 to 3.1. Seven (46.7%) patients had a complete response and were considered cured, 3 (20.0%) showed significant improvement, and 5 (33.3%) were classified as nonresponders. Urodynamic evidence of bladder instability, evident in all patients before treatment, was eliminated in 76.9% of patients. In all patients, mean total bladder capacity increased significantly from 197 to 252 ml, mean volume at first bladder sensa-

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tion increased from 95 to 133 ml, and mean bladder volume at normal desire to void increased from 133 to 188 ml. In the responding group, the mean total numbers of voids was reduced from 16.1 times during the day and 4.4 times during the night to 8.3 and 1.4 times, respectively. No complications from treatment were observed. Successful SANS treatment of nonobstructive urinary retention has also been reported, but further research for this indication is required.[8]

SANS neuromodulation is a safe and cost-effective method of neuromodulation that can easily be performed in the office. However, it does require multiple visits with a significant time commitment on the part of the patient. Although initial data reveal improvement in most parameters for urgency-frequency syndrome, urinary retention, and pelvic pain using peripheral percutaneous stimulation, it is still unclear if the results of short-term therapy are comparable to constant long-term implantable neuromodulation techniques. Further research in this area is necessary.

Interstim Central Sacral Nerve Stimulation

The Interstim Sacral Nerve Stimulation System (Medtronic Inc., Minneapolis, MN) was first introduced in Europe in 1994 and received Food and Drug Administration approval for use in urge incontinence in the United States in 1997 and then for urgency/frequency and nonobstructive urinary retention in 1999. The implantable system consists of a neurostimulator, an extension cable, and a lead with quadrapolar electrodes designed to be implanted at the S3 foramen to centrally neuromodulate bladder sensory afferents (Fig. 3). Candidates for the procedure initially undergo a bilateral needle test stimulation with temporary placement of a single electrode lead or a unilateral staged implant with secure implantation of the quadrapolar lead attached to an external stimulator. Patients are monitored postoperatively for 5 (needle test stimulation) to 30 (staged implant) days for symptomatic improvement based on an objective voiding diary or subjective patient assessment. Positive responders are considered for permanent implant while nonresponders have their test leads removed.

TECHNIQUE

Test stimulation to assess a patient's potential response to the permanent implant can be performed as needle test stimulation or staged implant. The bilateral needle stimulation has the advantage of being a mini-

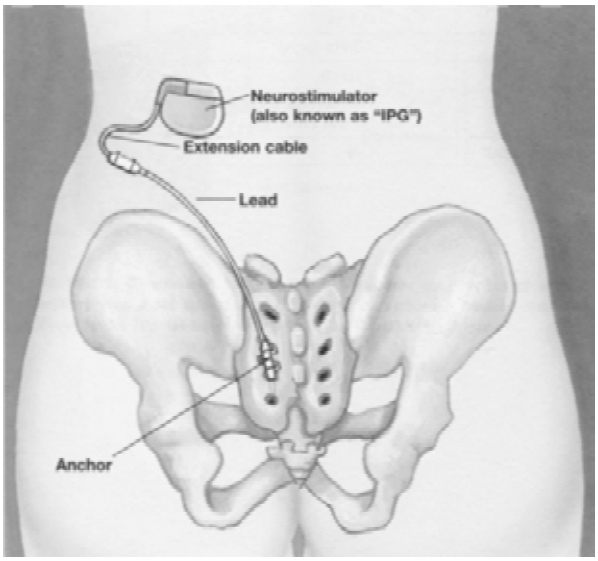

FIG. 3. Interstim implanted components – abdominal view.

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mally invasive percutaneous procedure with little risk. However, this test stimulation method has only one active lead on the wire and lacks secure attachment to prevent lead migration. The staged unilateral implant test stimulation has the advantages of a quadrapolar lead, secure attachment to the lumbodorsal fascia preventing lead migration, and longer test stimulation periods, thus increasing the chance of a positive response in potential implant candidates. Disadvantages of this approach include increased dissection (through a small paraspinal incision), increased risk of an intra- or postoperative morbidity, and the need for an additional procedure for lead removal in nonresponders. Choosing which test stimulation approach to perform depends on the counseling that takes place between the surgeon and the patient.

The needle test stimulation is performed under local anesthesia with the patient in the prone position. Materials used for the test stimulation are depicted in Figure 4. First, the grounding pad is applied to the skin just below the iliac crest at the edge of the postaxillary line. The sacrum and buttocks are prepared and draped to allow visualization of the pelvic floor for musculature response and feet for toe response to test stimulation. The bony landmarks of the sacrum are outlined with a sterile marker after confirmation using fluoroscopy (Fig. 5). A buffered local anesthetic is injected into the skin and subcutaneous tissues, and the bony surface of the sacrum is flooded bilaterally.

The foramen needle is used to pierce the skin at an acute angle 2 to 3 cm above the outlined S3 foramen mark, approaching the sacrum perpendicular to the bony surface. Repeated withdrawal and reinsertion of the needle with interval fluoroscopy is performed until the needle tip drops through the S3 foramen. Correct placement is confirmed with fluoroscopy (Fig. 6). The minihook is attached to the foramen needle and the test stimulator signal is gradually increased to obtain sensory or motor response. The position of the needle tip is adjusted as needed. A "bellows" response of the perineum and plantar flexion of the great toe and the patient's subjective "pulling in the rectum" confirms the correct position with stimulation of the S3 nerve root.

Once the optimal position has been determined, the stylus of the foramen needle is removed, and the test lead is threaded into the needle cannula until slight resistance is encountered, indicating that the lead has gone past the needle tip. Response is once

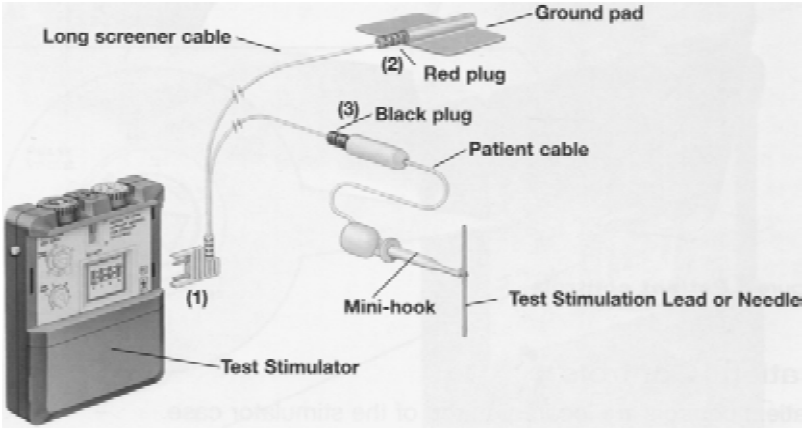

FIG. 4. Interstim needle test stimulation equipment.

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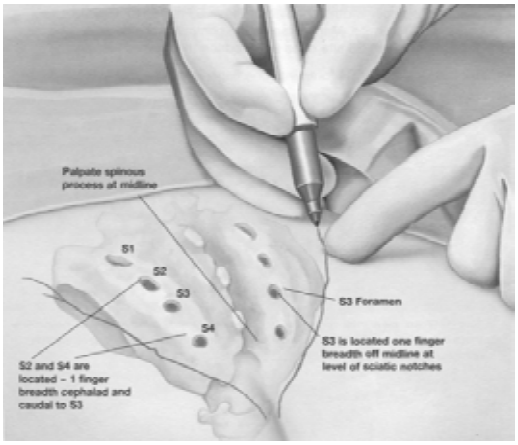

FIG. 5. The bony landmarks of the sacrum are outlined after fluoroscopic confirmation.

again confirmed and the needle is then removed while holding the stimulation lead firmly in place, minimizing migration of the tip. Lead response is then reconfirmed, and the lead is fixed to the skin with tape and further secured with a small, semipermeable transparent dressing. This procedure is repeated in an identical fashion on the contralateral side, and anteroposterior and lateral X-rays are performed to confirm and document lead position. The proximal end of the lead wire is connected to the black plug of the test stimulator that is worn by the patient on the belt or fanny pack during the test period. Patients are taught use and adjustment of the test stimulator and cautioned during this time to minimize aggressive activity that may cause lead migration.

The staged implant is an alternative technique of test stimulation with higher response rates due to more secure lead placement and availability of four stimulation leads at the wire tip. The procedure is to place a permanent lead followed by a second procedure for insertion of the subcutaneous implantable neurostimulator in those patients with a positive response. The unilateral staged implant test stimulation is performed on the side with greater response during needle stimulation. The initial steps of the staged implant technique are identical to the needle test stimulation. Once correct needle tip placement has been achieved under fluoroscopy with optimal motor and sensory response, a 6- to 9-cm paramedian incision is made with two thirds of the incision above, and one third of the incision below, the point of needle skin entry. The lumbodorsal fascia is exposed so that the needle is clearly visualized penetrating the fascia. Response is reconfirmed and the hub of the needle is then cut and an angiocath is threaded over the foramen needle to dilate the fascial hole. The foramen needle is removed and the quadrapolar lead is threaded through the angiocath sleeve. Flouroscopy and test stimulation of each electrode are used to confirm optimal position, adjusting the lead as necessary. Once correct placement is confirmed, the hub is slid onto the lead wire and locked in place. This hub is secured to the fascia with permanent sutures. The site is irrigated with an antibiotic solution (Fig. 7). A subcutaneous tunnel is created to the flank site using the tunneling tool and the lead is drawn to the site, secured with a transparent dressing, and connected to the external electrical stimulator. The incisions are closed. Patients are taught use and adjustment of the test stimulator and given precautions regarding pain, infection, and lead migration.

Patients with a positive response undergo full implant (following needle test stimulation) or subcutaneous placement of the implantable internal pulse generator (IPG) neurostimulator (following staged implant test stimulation). Placement of the permanent neurostimulator is a simple outpatient procedure that is performed in 15 to 20 minutes under local anesthesia. A subcutaneous pocket is made in the superior portion of the ipsilateral buttocks. Blunt dissection is performed to create a space that can easily accommodate the IPG. A subcutaneous tunnel is created from the IPG site to the previous flank incision and the extension connector is tunneled to the flank incision and attached to the lead wire with tightening screws. A pro-

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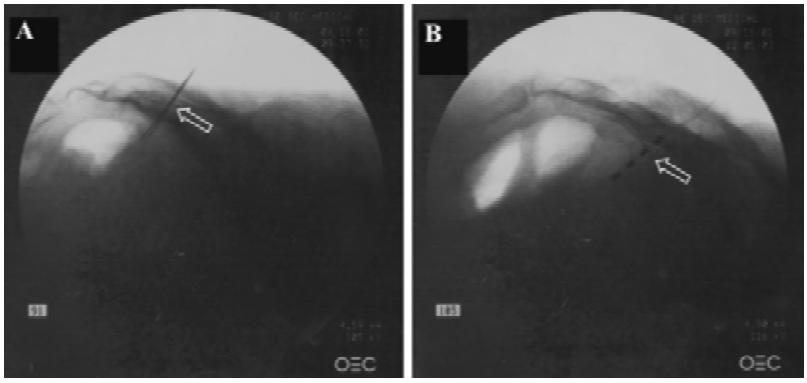

FIG. 6. Fluoroscopy confirming correct placement of (A) the foramen needle and (B) the quadrapolar permanent implant.

tective boot is slid over the lead connector assembly and secured with permanent suture. The other end of the connector is attached to the IPG and secured with tightening screws. The IPG is placed within the subcutaneous pocket, the incision is irrigated, and the skin is closed (Fig. 8). X-ray confirmation of lead and neurostimulator position is obtained. Patients are given discharge instructions and are told to return within 1 week for neurostimulator programming, which is performed in the office on an outpatient basis.

PATIENT PRECAUTIONS

In the immediate postoperative period, patients are advised to restrict activities for the first 3 to 6 weeks after surgery to minimize lead migration. They are also advised to turn off the neurostimulator while operating motor vehicles as a sudden change in perceived stimulation could cause a "startle" reaction that might affect safety. They are instructed to call their physician if they experience any signs of infection, change in bowel function, or pain.

These patients should be counseled that

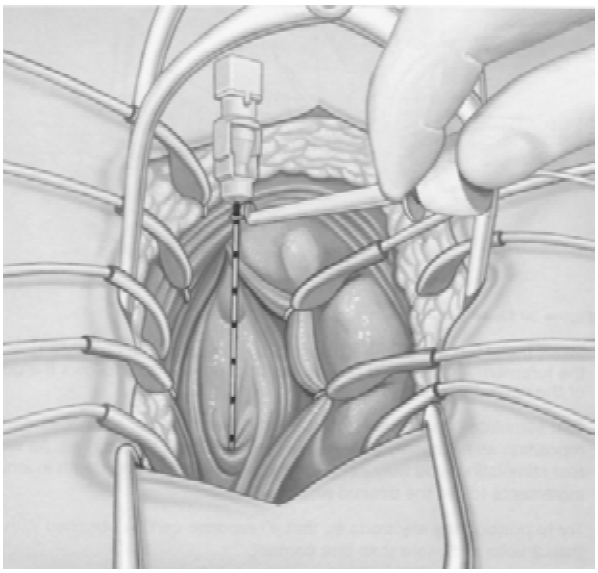

FIG. 7. Quadrapolar lead secured to lumbodorsal fascia after the correct position confirmed .

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FIG. 8. Placement of subcutaneous neurostimulator after positive test stimulation.

metal detectors and other security screening devices may cause the neurostimulator system to switch on or off or cause momentary increase in their perceived stimulation (ie, a "jolting" sensation). In addition, patients with this device should not undergo magnetic resonance imaging as it may change neurostimulator settings, damage the device, or injure the patient. This is an important consideration in patients with refractory OAB due to multiple sclerosis who undergo regular surveillance magnetic resonance imaging to monitor disease status. Electrocautery, external defibrillators, and ultrasound scanning equipment may also cause equipment malfunction and should be used with caution.

COMPLICATIONS

Complications are associated with the therapy, the device, or the procedure. These include pain at the implant sites, lead migration, infection or skin irritation, technical or device problems, transient electric shock, adverse change in bowel or voiding function, numbness, nerve injury, seroma at the neurostimulator site, change in menstrual cycle, and undesirable stimulation or sensations. Table 2 illustrates cumulative complication rates based on a multicenter trial of 581 patients with 914 test stimulations and 219 implants. The percutaneous needle test stimulation is safe with no reported major complications including nerve injury. The most common complication is lead migration, occurring in up to 15% of patients due to the tendency of the lead to move with activity as it is only taped in place. The perma-

TABLE 2. Complications Associated with Interstim Implant

Pain at the neurostimulator site (15.3%)
New pain (9%)
Suspected lead migration (8.4%)
Infection (6.1%)
Transient electric shock (5.5%)
Pain at lead site (5.4%)
Adverse change in bowel function (3%)
Technical problems (1.7%)
Suspected device problem (1.6%)
Change in menstrual cycle (1%)
Adverse change in voiding function (0.6%)
Persistent skin irritation (0.5%)
Suspected nerve injury (0.5%)
Device rejection (0.5%)

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nent implant has, unfortunately, been associated with higher complication rates and need for surgical revision. There have been no reports of serious adverse device effects or permanent injury associated with the device or the use of sacral nerve stimulation. In earlier studies, the revision rate including device explantation, IPG exchange, and repositioning of the lead electrode was as high as 33% (51/157 patients). Studies have shown that probability of revision decreases with surgical experience with 29% in the first year and dropping to 12% in the second year. This decrease may represent complications associated with the learning curve for this novel procedure.[9] With recent advances in technique and technology, the incidence of these complications has been significantly reduced. Overall, the technique is safe with few significant or permanent adverse effects.

RESULTS

Despite the recent introduction of the technique, there is a growing amount of literature regarding its efficacy in the treatment of OAB, urinary retention, and interstitial cystitis/pelvic pain. Device implantation is being performed worldwide with increasing experience regarding outcomes and complications.

The role of central neuromodulation in the treatment of OAB is well established. As early as 1993, Djkema et al[10] reported their initial experience with an implanted neuroprosthesis stimulating the S3 nerve root in 23 women with refractory voiding dysfunction. Nineteen of the 23 women reported greater than 50% improvement in their symptoms at median follow-up of 12 months. The number of daily urge incontinent episodes decreased from 7.4 to 1.5 per day and functional bladder capacity increased from 135 to 227 ml.

Long-term effectiveness of the Interstim system for refractory urge incontinence was recently assessed by Janknegt et al[11] in the Netherlands study group. Compared with baseline, a group of 96 implanted patients demonstrated significant reductions in the number of urge incontinent episodes per day, severity of leaking, and the number of absorbent pads/diapers replaced per day due to incontinence at an average of 30.8 ± 14.8 months. Eleven of the 96 patients underwent device explant due to lack of efficacy, pain, or bowel dysfunction. Improvement of OAB symptoms in patients with detrusor hyperreflexia due to neurologic causes (eg, spinal cord injury, multiple sclerosis) has also been reported, but patients should be counseled that the results of therapy may deteriorate with time if the have a progressively worsening neurologic condition.

Perhaps one of the most encouraging applications for central neuromodulation is the treatment of nonobstructive urinary retention. Previous to this therapy, traditional treatment options were restricted to medications and catheterization with uniformly poor results. In 1998, Shaker and Hassouna[12] reported their experience in 20 patients (age 19 to 56 years) with idiopathic nonobstructive urinary retention. Test stimulation was performed and responders underwent implantation. The patients were followed for 1, 3, and 6 months postoperatively, and every 6 months thereafter. Sacral root neuromodulation restored voiding capability in all patients. Postvoid residual urine decreased from 78.3 to 5.5 ml. The mean postprocedure residual corresponded to only 10.2% of the total prevoid bladder volume, which is considered to be within the normal range. These results were reflected in uroflowmetry and pressure-flow studies, which were almost always normal after implantation. Furthermore, the urinary tract infection rate decreased significantly and associated pelvic pain improved substantially.[12]

Jonas et al[13] and the German study group recently published a randomized prospective trial of 177 patients with refractory urinary retention with follow-up evaluations including voiding diary and temporary deactivation of the implant in the treatment group at 3, 6, 12, and 18 months. Compared with

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the control group, patients implanted with the InterStim system had statistically significant reductions in the catheter volume per catheterization. Of the patients treated with implants, 69% eliminated catheterization at 6 months and an additional 14% had a 50% or greater reduction in catheter volume per catheterization. Success was achieved in 83% of the implant group with retention compared with 9% of the control group at 6 months. Temporary inactivation of sacral nerve stimulation therapy resulted in a significant increase in residual volumes ($P < 0.0001$), but the effectiveness of sacral nerve stimulation was sustained through 18 months after implant.[13]

The largest study to date was the multicenter trial published by Siegel et al[14] that analyzed 581 patients: 184 with urge incontinence, 220 with urgency-frequency, and 177 with urinary retention. All patients were refractory to previous traditional therapies. Of the 581 patients, 260 had a successful test stimulation procedure and 219 eventually underwent implant. Patients were evaluated at 6-month intervals using detailed quantitative voiding diaries. For urge incontinence, successful outcome, defined as dryness or greater than 50% reduction in leakage episodes, was achieved in 75%, 79%, and 76% of patients at 6, 12, and 18 months postimplant, respectively. Similarly, urgency-frequency patients reported 48%, 64%, and 63% success rates at the same intervals when measuring reduction in voids per day. Improvement in urgency in this group was noted to be 83%, 82%, and 79% at 6, 12, and 18 months, respectively. Success in the treatment of urinary retention, defined as elimination of the need for catheterization or greater than 50 reduction in catheterization episodes, was reported to be 72%, 77%, and 71%, respectively, at the same intervals. No permanent adverse effects were noted. Complications associated with therapy in this group have been previously described (Table 2).

There is limited data regarding the use of central neuromodulation in the treatment of interstitial cystitis and pelvic pain. Caraballo et al[15] reported their early experience in patients with OAB and pelvic pain. In the ten patients with pelvic pain, 3 (30%) had no or minimal improvement, 5 (50%) had marked improvement, and 2 (20%) were cured based on subjective analysis. Maher et al[16] reported similar improvement in women with interstitial cystitis undergoing the needle test stimulation procedure. Fifteen women with refractory interstitial cystitis with a mean duration of symptoms of 5.2 years underwent percutaneous stimulation. Mean voided volume during treatment increased, and mean daytime frequency and nocturia decreased significantly. Mean bladder pain decreased from 8.9 to 2.4 points on a scale of 0 to 10. As indicated by the Short Urinary Distress Inventory and SF-36 Health Survey, the quality-of-life parameters of social functioning, bodily pain, and general health significantly improved during the stimulation period. Of the women, 73% requested to proceed to complete sacral nerve root implantation. Given the poor outcomes in patients with interstitial cystitis and chronic pelvic pain syndromes with traditional treatment options, these initial results are encouraging and further research for this off label application is currently in progress.

Clinical Treatment Algorithm

Evaluation and management of voiding dysfunction, OAB, and urinary retention need to be individualized for each patient and will often depend on the clinician's experience and available resources. A step-by-step treatment algorithm that includes history, physical exam, and appropriate office testing is useful as a guide in the evaluation of the female patient with voiding dysfunction. (Tables 3 and 4) All patients should initially undergo a detailed medical history, which should focus on the duration, characteristics, and severity of the presenting symptoms with particular attention to precipitating factors and reversible causes. Antecedent ob-

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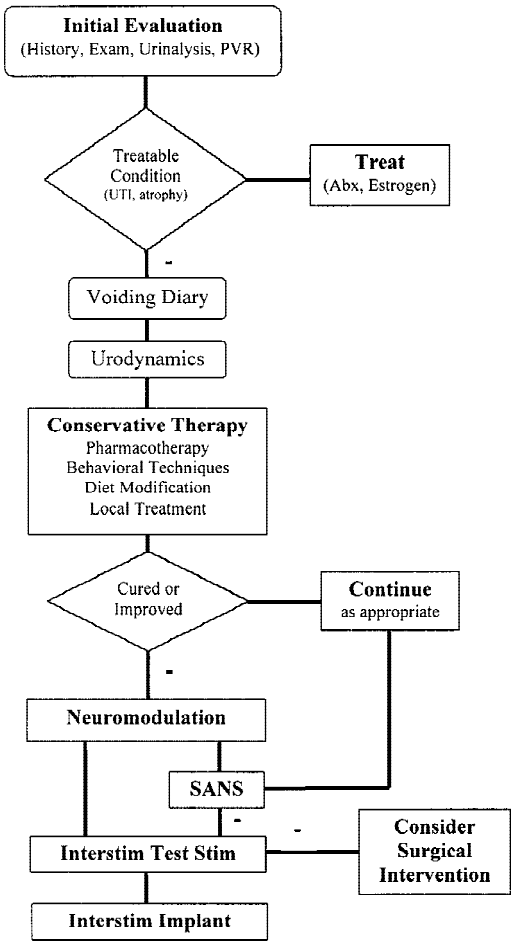
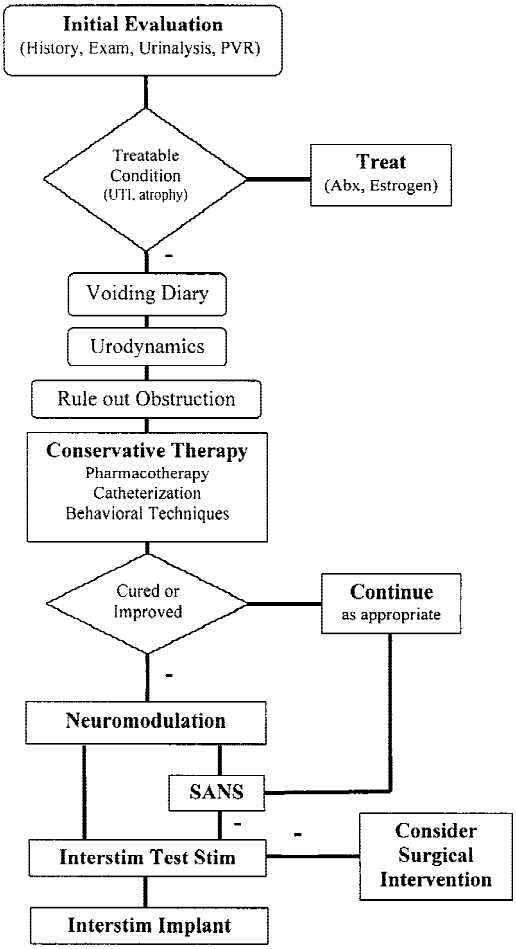
TABLE 3. Treatment Algorithm for Overactive Bladder Syndrome



PVR = postvoid residual; SANS = Stoller Afferent Nerve Stimulator; UTI = urinary tract infection.

stetrical, medical, and surgical history can be helpful in determining etiologic factors. Physical assessment, including mental status, neurologic, and pelvic exams will often provide additional information and supporting data. Initial labs may include urinalysis, urine cytology, and measurement of a postvoid residual (PVR). In select patients, additional testing with a voiding diary and/or urodynamic evaluation may be indicated. Conservative measures are instituted after an acute treatable condition (like lower urinary tract infection) is excluded. Although some physicians prefer an incremental addition of therapies, the authors recommend a multimodal approach combining pharmacotherapy, behavioral training, and diet modification from the onset as this approach is associated with faster and greater response.[17] This combined approach also reduces failure due to patient noncompliance and provides an integrated approach to the multifactorial pathogenesis of voiding dysfunction. Patients should be routinely evaluated at regular intervals with the use of periodic voiding diaries to provide documentation of response. Nonresponders should have the treatment protocol modified

TABLE 4. Treatment Algorithm for Urinary Retention



See Table 3 for definitions.

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with increased training intervals or medication dose adjustment.

Neuromodulation is offered to patients depending on the clinician's comfort level and past experience. Treatment recommendations should be customized to each patient's clinical presentation, and the authors often offer patients neuromodulation on the first visit if they have previously failed other conservative approaches or decline pharmacotherapy. Choice of neuromodulation technique will depend on various factors including severity of symptoms, coexisting medical conditions, and patient desires. Most patients initially prefer office-based peripheral neuromodulation as it is extremely safe and convenient and seems to be an excellent introduction to the concept of neuromodulation. Those patients with poor response or requiring prolonged treatments are offered the Interstim test stimulation and possible permanent implant. Some patients opt to go directly to the Interstim test stimulation after counseling and discussion of risks and benefits. Appropriate treatment algorithms will vary among physicians and will often change with growing experience.

Future Directions

Sacral neuromodulation seems to be an effective treatment option for patients with refractory voiding dysfunction. Although the exact mechanism of action is incompletely understood, it is theorized that electrical stimulation modulates somatic afferent inhibition of sensory processes. The procedure can be performed using peripheral percutaneous acupuncture or a central implantable neurostimulator. Risks and benefits of these two approaches vary and there is no data regarding comparative efficacy or safety. Long-term results of the Interstim implant are encouraging and hold great promise for patients.

Sacral neuromodulation may ultimately prove to be a significant advance in the understanding and ability to treat various conditions related to the pelvic floor. The role of the nervous system in various disease processes is only beginning to be understood and it is expected that the knowledge base will increase with time. With improved understanding, the technique and results should improve and the indications should broaden. Currently, major limitations are related to the infancy of this field. Little work has been performed for technical or procedural improvement of the peripheral neuromodulator. Possible options include a miniature peripheral implant and protocol revisions regarding frequency and tapering of treatments. The equipment presently used for central neuromodulation has been adapted from other fields and various technique issues, like improved response from bilateral use, remain unanswered. Already, the implant procedure has been modified, resulting in fewer complications and better long-term outcomes. The role of adjunct pharmacotherapy and behavioral modification is still unclear. Use of neuromodulation as a primary treatment in all patients or certain subsets has not been studied. Factors identifying patients likely to respond are unknown. Costs of the procedure and associated equipment remain high and availability to patients is restricted by the relatively few number of physicians performing the procedure. Finally, reimbursement for the procedure has been inconsistent and is only now being covered by most third-party payors. Previous to widespread acceptance, further data addressing these important issues is required. With greater understanding of the mechanism of neuromodulation, improved technology, and increased experience, neuromodulation may become the mainstay for the treatment of all patients with OAB, urinary retention, and pelvic pain. Until then, it is a promising option for the difficult patient refractory to conventional therapies.

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