Overactive bladder: Recognition requires vigilance for symptoms

■ ABSTRACT
Overactive bladder (OAB) is a prevalent condition in both men and women that imposes significant burdens on the patient and his or her quality of life. Nevertheless, only a small percentage of patients with OAB receive diagnosis and treatment. The identification of OAB is well within the scope of the primary care provider, as it is symptom-based and does not generally require specialized testing. The treatment of OAB relies on behavioral modification and/or pharmacologic options, primarily antimuscarinic therapy. Better identification of OAB symptoms in the primary care setting should reduce the number of patients suffering from untreated OAB.

■ DEFINITION OF THE CONDITION
Overactive bladder (OAB) is defined by the International Continence Society as a symptom complex of urinary urgency (intense, sudden desire to void) with or without incontinence, urinary frequency (voiding eight or more times in a 24-hour period), or nocturia (awakening at night to void). The symptoms of OAB are present in the absence of any pathologic or metabolic disorders that could cause them.

Although this paper deals primarily with OAB, it is important to recognize other types of lower urinary tract symptoms (LUTS) and dysfunctions that could cause them.

Most cases go untreated
Despite the large number of both men and women with OAB, only 15% of all patients with symptoms of OAB receive treatment. Kinchen and colleagues noted that only one of four women with symptoms of OAB with UI seeks clinical help.

Patients want their primary care provider (PCP) to discuss the issue, yet there appears to be a communication gap. A recent online survey of 1,228 women aged 40 to 65 years (898 of whom had symptoms of OAB) found that more than half of the women who discussed OAB with a health care provider (56%) waited longer than 1 year to seek treatment; many attempted self-management of their symptoms. A contributing factor is the stigma surrounding bladder control problems and the many misconceptions that patients have about their condition that may prevent them from seeking care.

Social cost of OAB
OAB significantly affects many aspects of a patient’s life, including self-esteem, sexual relations, family...
relations, lifestyle, professional life, health perception, and sleep.9 “Bathroom mapping” is a common behavioral technique of patients with OAB. Since they need to void frequently, they will consciously or unconsciously conduct a search for all the bathrooms in the vicinity in order to prevent an emergency. It is not uncommon for OAB patients to avoid prolonged social activities so as not to embarrass themselves with the frequency of toilet use.

Financial cost of OAB: Direct, indirect, and intangible
The social implications of OAB can be explained by its direct, indirect, and intangible costs. Direct costs include those associated with treatment, diagnosis, routine care, and the consequences of the disease. Indirect costs encompass lost wages and productivity. Intangible costs are associated with suffering, embarrassment, and overall decreased quality of life.11

A study by Hu et al estimated that the direct cost of OAB in the United States was $12.6 billion during 2000.12 Although providers are familiar with the costs of treatment and routine care of OAB, they may not be as aware of the costs associated with the consequences of the disease, which make up greater than 50% of the overall costs. These consequences include skin irritation, urinary tract infections, falls, additional admissions to institutions, and prolonged hospital stays.13 The odds ratio of a hip fracture is two times greater in an elderly woman with urge UI than in the general population.14 One can only speculate on the reason for this increased risk; however, the authors have treated OAB patients who have tripped in a dark room as they raced to the bathroom and others who have slipped in a urine puddle on their way back.

The indirect costs and intangible costs of OAB are more difficult to quantify. It may be helpful to think of the indirect costs as the wages lost to missed work as a result of OAB or the decreased productivity from continually needing to find the bathroom. Although intangible costs defy being assigned an actual price by their very definition, they nevertheless can be devastating. In a national community survey, Coyne et al reported that both continent and incontinent OAB patients suffered in all health-related quality-of-life measures compared with controls who did not have OAB.15 Additionally, the prevalence of depression is markedly higher in patients suffering OAB, with or without UI, than in the general population.8

Although the social implications of OAB clearly reflect a large societal burden, there is good news in the form of opportunities for intervention in treatment-naïve patients. A 2006 study by Balkrishnan et al shows that compliance with medications for OAB can result in a significant decrease in older adults’ health care costs.16

PATHOGENESIS
OAB is a syndrome with a varied pathophysiology that may be multifactorial. The detrusor is composed of smooth muscle under voluntary neurologic control. Idiopathic OAB has been proposed to be secondary to myogenic or subclinical neurogenic abnormalities. A “neurogenic bladder” is a result of neurologic dysfunction. Although the etiology of OAB is not clear, the cause of its symptoms is better understood and will be reviewed below.

How the bladder normally functions
To understand the abnormal function suffered by the patient with OAB, it is instructive to first review normal bladder function. Micturition involves two important and discrete processes: (1) bladder filling and storage, and (2) bladder emptying.17 The filling and storage phase requires accommodation of increasing volumes of urine at low intravesical pressures with appropriate sensation, a closed bladder outlet (adequate outlet resistance), and absence of involuntary contractions (which result in urgency or leakage). The process of
bladder emptying requires a coordinated contraction of the bladder muscle, a lowering of the resistance of the outlet (sphincter), and an absence of anatomic obstruction. All types of voiding dysfunctions may be classified by an abnormality of one or more of the factors listed, alone or in combination.

Although its specific etiology is not known, OAB can be explained as the inability to accommodate increasing volumes of urine as a result of high intravesical pressures, along with increased sensation causing symptoms of urgency and frequency with or without a contraction.

### Abnormal urge sensation in OAB

In the OAB patient, signals to the bladder allow contraction and subsequent micturition before the bladder reaches full capacity. When this signal is sudden, intense, and difficult to deter, patients report the urgency associated with OAB. This is opposed to a normal urge sensation that allows the patient adequate warning to prepare for bladder emptying. Whether this abnormal signaling is an amplification (ie, increased sensitivity) of the afferent “sensory” fibers or increased output of the efferent motor fibers is not known.

Antimuscarinic therapy aims to block these pathways from overresponding, as discussed below.

### OAB, benign prostatic hyperplasia, and bladder outlet obstruction are interrelated

In discussing the pathophysiology of OAB, the connection between OAB, benign prostatic hyperplasia (BPH), and bladder outlet obstruction is important to note. The incidence of OAB increases with age, and many men develop OAB symptoms concomitantly with BPH. The most common cause of voiding symptoms in men is related to urethral obstruction from the prostate gland, secondary to BPH. Approximately 50% of men with some type of prostatic obstruction also have detrusor overactivity, but conversely, men younger than 60 years who present with LUTS tend not to have an enlarged prostate or a history of BPH. The relationship between symptoms and OAB, bladder outlet obstruction, and BPH remains unclear.

### EVALUATION

The evaluation of the patient with OAB should focus on the history, the physical examination, and a limited laboratory evaluation. During the physical examination, it is useful to pay attention to items that may be transient or reversible.

### Screen for symptoms

The history may be the most important component in the evaluation of the patient with OAB, and the symptoms of urgency, frequency, nocturia, and UI are paramount. Screening for OAB requires minimal time from a provider, as a self-administered screener or questionnaire can be used in most clinical settings. In this context, a screening tool or questionnaire is not meant to diagnose OAB or UI, but rather to identify symptoms that may require treatment. Onset, duration, severity, and bother can be noted with a few key questions. Table 1 lists examples of questions that may be useful.

### Components of the history

A full neurologic history should be taken to explore the possibility of dementia, Parkinson disease, spinal cord injury or stenosis, multiple sclerosis, or stroke. Functional and cognitive assessment should be performed in older patients.

The gastrointestinal history is important, as constipation can cause OAB and the medications used to treat OAB can cause or exacerbate constipation. Dietary habits, especially regarding fluid intake, have long been thought to be associated with urinary symptoms and should be addressed in the history. A relationship between LUTS and consumption of caffeinated beverages or alcohol is often seen in clinical
practice, although there is a lack of clear-cut data supporting such a relationship, except with tea con-
sumption.26

Prior surgeries need to be considered, especially any genitourinary interventions (eg, hysterectomy or
bladder suspensions). Orthopedic procedures can be the cause of transient OAB as a result of temporary
mobility issues.

Obstetrical history should be addressed in women, as a history of several or difficult vaginal deliveries
can predispose a woman to OAB or stress UI.

Medications should be reviewed to explore a potential association with symptoms. For example, the
timing of when a diuretic is taken can have profound effects on urinary habits.2 Medications that can affect
urinary function are listed in Table 2.27

Pearls for conducting the physical exam
The physical examination should focus on detecting anatomic and neurologic abnormalities that could con-
tribute to the patient’s symptoms. The neurologic examination should start by observing the patient’s gait as he
or she walks into the room or down the hall. Limping, poor coordination, dysarthria, facial asymmetry, or other
findings may indicate neurologic conditions such as a stroke or multiple sclerosis. A brief mental status exam-
ination can be performed by observing the patient’s general appearance and his or her response to questions.
Alertness, orientation, memory, and thought content can be useful parameters in patient assessment.

**TABLE 1**
Simple screening questions for evaluation of overactive bladder (OAB) and incontinence

<table>
<thead>
<tr>
<th>Question</th>
<th>Suggests</th>
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<tbody>
<tr>
<td>Do you get sudden urges to go to the bathroom that are so strong you can’t ignore them?</td>
<td>OAB/UUI</td>
</tr>
<tr>
<td>How often do you go to the bathroom? More than eight times in a 24-hour period?</td>
<td>OAB</td>
</tr>
<tr>
<td>Do you have uncontrollable urges to urinate that sometimes result in wetting accidents?</td>
<td>OAB/UUI</td>
</tr>
<tr>
<td>Do you leak urine on the way to the bathroom?</td>
<td>UUI</td>
</tr>
<tr>
<td>Do you frequently get up two or more times during the night to go to the bathroom?</td>
<td>OAB</td>
</tr>
<tr>
<td>Do you avoid places that you think won’t have a nearby restroom?</td>
<td>OAB/UUI</td>
</tr>
<tr>
<td>When you’re in an unfamiliar place, do you make sure you know where the restroom is?</td>
<td>OAB/UUI</td>
</tr>
<tr>
<td>Do you leak urine when you laugh, cough, or sneeze?</td>
<td>SUI</td>
</tr>
<tr>
<td>Do you use absorbent pads to keep from wetting your clothes?</td>
<td>SUI or UUI</td>
</tr>
</tbody>
</table>

UUI = urge urinary incontinence; SUI = stress urinary incontinence

Adapted, with permission, from Newman DK, Giovannini D. The overactive bladder: a nursing perspective. Am J Nurs 2002; 102:36–45.23

**TABLE 2**
Medications that affect bladder function

<table>
<thead>
<tr>
<th>Medication</th>
<th>Effect</th>
</tr>
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<tbody>
<tr>
<td>ACE inhibitors</td>
<td>Cough leading to stress UI</td>
</tr>
<tr>
<td>Alpha-adrenergic agonists</td>
<td>Increased urethral resistance, causing postvoid dribbling, straining, hesitancy in urine flow</td>
</tr>
<tr>
<td>Alpha-receptor agonists (pseudoephedrine, ephedrine)</td>
<td>Urethral constriction, urinary retention (males)</td>
</tr>
<tr>
<td>Alpha-receptor antagonists</td>
<td>Urethral relaxation and decreased urethral resistance, causing stress UI (females) and UI with cough, sneeze, or other activity</td>
</tr>
<tr>
<td>Anticholinergics (H1 antihistamines, antiparkinsonian agents)</td>
<td>Urinary retention with symptoms of postvoid dribbling, straining, hesitancy in urine flow, overflow incontinence, fecal impaction</td>
</tr>
<tr>
<td>Antipsychotics/sedatives</td>
<td>Sedative effect, causing confusion; may relax detrusor muscle, leading to urinary retention</td>
</tr>
<tr>
<td>Beta-receptor antagonists</td>
<td>Urinary retention</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>Urinary retention, fecal impaction</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Increased urine production (polyuria) and volume, leading to urgency and frequency</td>
</tr>
<tr>
<td>Methylxanthines (caffeine, theophylline)</td>
<td>Polyuria, bladder irritation</td>
</tr>
<tr>
<td>Neuroleptics (thioridazine, chlorpromazine)</td>
<td>Anticholinergic effect, sedation</td>
</tr>
<tr>
<td>Other (caffeine and alcohol)</td>
<td>Diuretic effect, leading to urgency and frequency; possible sedation</td>
</tr>
<tr>
<td>Opioids</td>
<td>Urinary retention, fecal impaction, sedation, delirium</td>
</tr>
<tr>
<td>Sedatives and hypnotics</td>
<td>Sedative effect, which may relax detrusor muscle</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>Anticholinergic and alpha-receptor antagonist effects, causing postvoid dribbling, straining, hesitancy in urine flow</td>
</tr>
</tbody>
</table>

UI = urinary incontinence

Adapted from Newman.27
If the patient appears overweight, consider calculating the body mass index (BMI). The relationship between increased BMI (> 30 kg/m²) and the likelihood of UI in females is strong. Identifying this correlation provides an opportunity for the PCP to discuss lifestyle changes with the patient, as research has shown that moderately obese women who lose 5% to 10% of their weight have a decrease in LUTS.

Check the abdomen for masses, hernias, or a distended bladder. In women, the genitalia should be assessed for abnormalities such as prolapse of the bladder or uterus, atrophic vaginitis, or urogenital atrophy, and rectal sphincter tone should be checked. It may be useful to examine the female patient when her bladder is full in order to identify stress UI. In men, assess prostate size (an enlarged prostate can lead to OAB symptoms), the penis and scrotum for abnormalities (such as urethral discharge, epididymitis, or even urethral stricture), and rectal sphincter tone. A basic neurologic examination focusing on motor and sensory components (eg, anal wink and bulbocavernosus reflex) should be performed.

A voiding diary is a simple and practical method of obtaining detailed information about a patient’s voiding habits, and can be helpful in evaluating the extent of the problem and offering clues on how best to proceed with evaluation and treatment. The diary or log should be structured to keep track of voiding, urgency, and UI patterns over a 3-day period (Figure 1).

**Judicious use of ancillary studies**

The number of ancillary studies required is controversial. It may be prudent to check chemistries, especially renal function and blood glucose, in certain patients. For example, the onset of polyuria/polydipsia in the diabetic patient could certainly mimic the symptoms of OAB. Furthermore, if the clinician suspects obstruction in a man, renal function studies may identify upper urinary tract involvement. A urinalysis should be performed to rule out urinary tract infection. Many elderly women will have asymptomatic bacteriuria that does not require treatment. The role of further studies is questionable.

Checking the patient’s postvoid residual urine volume using portable ultrasonographic equipment is useful for detecting retention, but it has a limited role in the neurologically normal female. In the male, it becomes more important because the symptoms of a large, obstructing prostate are similar to those of OAB. A postvoid residual volume check is necessary in any patient in whom there is concern about incomplete bladder empting as a result of neurologic dysfunction, anatomic abnormality, or a pharmacologic cause. It is also necessary in the postoperative patient who develops OAB. The incidence of postoperative urinary retention is recognized but poorly understood, with rates ranging from 4% to 25%. Some patients may present in frank retention, whereas others may present with OAB symptoms from incomplete emptying.

Urodynamic studies are not necessary in most patients, especially those without neurologic compromise. If the patient’s symptoms are refractory to therapy, if they worsen, or if there is significant postvoid residual volume, then urodynamic studies may be considered as one looks for other causes, such as detrusor sphincter dyssynergia. In our view, a significant postvoid residual volume is any amount greater than 75 to 100 mL in persons younger than 65 years; in the elderly, we consider a volume less than 150 mL to be acceptable. There are no studies supporting specific values for acceptable postvoid residual volume, but there are guidelines.

Cystoscopy has a role only in the patient with hematuria or the patient who is refractory to therapy.
Radiologic evaluation beyond portable bladder ultrasonography is reserved for those with hematuria or a palpable mass noted on examination.

Differential Diagnosis

As mentioned, the diagnosis of OAB can be based on symptoms. As with any symptom complex, however, a differential diagnosis should be considered. A history combined with a directed physical examination, urinalysis, and chemistries will exclude most of the alternate diagnoses listed in Table 3. Table 4 presents findings that should prompt further evaluation or referral to a specialist.

Treatment

The goal of treatment is to teach the patient to inhibit urgency and to improve voluntary control over bladder function.

Behavioral treatment

Behavioral modification involves educating patients about the normal process of micturition and how their specific symptoms define an abnormal situation. If patients are actively involved in the diagnosis and subsequent treatment, their expectations are more readily attainable.

Behavioral therapy may involve pelvic floor muscle exercises, bladder retraining and urge-suppression techniques, changing the timing of various medications (eg, diuretics), or encouraging exercise and weight loss. Although most patients will be treated using drug therapy, the combination of behavioral and pharmacologic therapies greatly enhances the likelihood of a positive outcome compared with either intervention alone. Burgio et al conducted a crossover study among older women with UI to assess the effects of behavioral therapy, drug therapy, and their combination on patients’ baseline frequency of UI episodes. Patients receiving behavioral therapy alone in the initial study phase had a 57% reduction in the frequency of UI, which increased to an 89% reduction after the addition of drug therapy. Similarly, patients receiving drug therapy alone in the initial phase had a 73% reduction in the frequency of UI, which increased to an 84% reduction after the addition of behavioral therapy. The authors concluded that combination therapy yields better outcomes.

Pharmacologic management:

Antimuscarinics are first-line

The principle behind pharmacologic management of OAB is inhibition of the disturbed bladder contraction, and the antimuscarinics are the primary medications used for this effect.

Antimuscarinics exert their clinical effect through two potential pathways: one on the motor pathway via central and peripheral actions that block a facilitatory mechanism and stimulate an inhibitory mechanism; and the other on the sensory pathway via central and peripheral actions that modulate afferent innervations.

As a class, antimuscarinics are safe and effective. Comparisons among these agents have been limited, but, as with any drug class, there are subtle differences that PCPs should be aware of. Dose adjustment, side effects, or metabolism may be important to consider on an agent-by-agent basis for the individual patient. The various antimuscarinics and their properties are detailed in Table 5. All of these agents are administered orally; in addition, oxybutynin is also available for delivery by transdermal patch.

Most antimuscarinics have not been directly compared in clinical trials, and outcome measures and patient characteristics differ between trials, making comparisons difficult. Two comparative efficacy studies deserve attention, the OPERA (Overactive Bladder: Performance of Extended Release Agents) trial and the STAR (Solifenacin and Tolterodine as an Active Comparator in a Randomised) trial. The OPERA trial compared the long-acting oral versions of oxybutynin (10 mg) and tolterodine (4 mg). There was a reduction of UI with oxybutynin

<table>
<thead>
<tr>
<th>TABLE 3</th>
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<tbody>
<tr>
<td>Differential diagnosis of symptoms suggestive of overactive bladder</td>
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</table>

<table>
<thead>
<tr>
<th>In women</th>
<th>In men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary tract infection</td>
<td>Benign prostatic hyperplasia</td>
</tr>
<tr>
<td>Prolapse</td>
<td>Bladder outlet obstruction</td>
</tr>
<tr>
<td>Urethral obstruction</td>
<td>Urethral stricture</td>
</tr>
<tr>
<td>Atrophic vaginitis</td>
<td>Bladder stones</td>
</tr>
<tr>
<td>Bladder cancer</td>
<td>Bladder cancer</td>
</tr>
<tr>
<td>Interstitial cystitis</td>
<td>Prostate cancer</td>
</tr>
<tr>
<td>Postsurgical incontinence</td>
<td>Diabetes</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>Medications/diuretics</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>Neurogenic bladder</td>
</tr>
<tr>
<td>Medications/diuretics</td>
<td>Postsurgical incontinence</td>
</tr>
<tr>
<td>Neurogenic bladder</td>
<td></td>
</tr>
</tbody>
</table>

Recent pelvic surgery

Stress urinary incontinence

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over tolterodine, but it came at a slight and almost proportional increase in dry mouth.33

The STAR trial compared a single dosage strength of long-acting tolterodine (4 mg) with a flexible-dose regimen of solifenacin (5 or 10 mg). Using pooled data for the two solifenacin doses, the study found that titratable solifenacin was associated with slightly better efficacy than tolterodine with an almost proportional increase in side effects.34

Another recent head-to-head study compared the effects of darifenacin (7.5 mg) and long-acting oral oxybutynin (10 mg) on cognitive end points in subjects 60 years of age or older.35 The premise of the study was that an agent with selectivity for the M3 receptor (the prominent muscarinic receptor on the bladder) would not affect the M1 receptors in the brain. The outcome studied was performance on the Name-Face Association Test, which measures delayed recall, at week 3 of treatment. Subjects randomized to oxybutynin performed statistically worse on this test than did placebo recipients, indicating significant memory impairment, whereas no reduction in performance was seen in darifenacin recipients.35

Secondary medications
Although the antimuscarinic class is the first line of pharmacologic therapy for OAB, other medications have a role. There is some evidence that the stress component of mixed UI may respond to the tricyclic antidepressant imipramine or to an alpha-adrenergic agonist such as pseudoephedrine, which increases outlet resistance.36 Furthermore, these drugs may work synergistically with antimuscarinic therapy in patients with mixed UI. However, imipramine is not indicated in the elderly and pseudoephedrine should be used with caution in the elderly. Treatment should be geared to the symptom that appears to be most bothersome.37 Neither imipramine nor pseudoephedrine is approved by the US Food and Drug Administration for treating OAB or stress UI.

Transvaginal estrogen therapy also may have a role in treating the irritative symptoms of urgency and frequency associated with vaginal and urogenital atrophy; however, data are lacking to support any particular dosing regimen, route of administration, or treatment duration.38 A recent analysis from the Women’s Health Initiative found that oral estrogen replacement not only failed to improve UI but may actually worsen symptoms.39

Risk of urinary retention with therapy is low
A common concern among FCPs is that antimuscarinic therapy may place a patient at risk of urinary retention. However, the incidence of retention in both men and women in clinical trials is low.40 Kaplan et al evaluated the safety and efficacy of antimuscarinic therapy in men with BPH and LUTS in whom alpha-antagonist therapy failed to relieve LUTS.40 In the 39 men who completed this 6-month trial, there was a significant decrease in urinary frequency, nocturia, and postvoid residual volume, as well as an improvement in symptom scores. There were no reports of urinary retention. These findings suggest that the inhibitory effect of antimuscarinic agents on detrusor muscle contraction is unlikely to aggravate voiding difficulties in men with OAB symptoms and possible obstruction.

We believe it is prudent to do a postvoid residual volume check in a man being treated for LUTS, both initially and at follow-up. However, this practice is controversial, and the most appropriate candidates for these checks remain to be better defined.

Symptom-based treatment can be successful
This paper has addressed the empiric diagnosis and treatment of OAB. The concept of empiric diagnosis and treatment was assessed in the recently published IMPACT (Improvement in Patients: Assessing Symptomatic Control with Tolterodine) trial.41 In this study, the diagnosis of OAB was made in several hundred patients in primary care and obstetric/gynecologic offices on the basis of symptoms. Patients with OAB symptoms for at least 3 months were treated with extended-release tolterodine for 12 weeks in this
open-label, single-arm trial. At the end of the 12 weeks, there were significant reductions from baseline in urge UI, urgency episodes, nocturnal frequency, and daytime frequency. Common side effects were dry mouth and constipation.

The conclusion drawn from this paper was that patients with OAB in the general population can be readily screened and successfully treated with minimal work-up. The applicability to the PCP is significant, but the study lasted only 12 weeks and longer follow-up would have been useful.

## APPROPRIATE FOLLOW-UP

There is no set rule as to the follow-up interval for the OAB patient. Some clinicians find that a 2-week interval is adequate, whereas others recommend 4 weeks. The interval should be determined by consensus of the provider and the patient. The patient must be educated about what to expect and to not give up hope if these expectations are not met immediately, as a simple drug change or dose titration may provide the desired effect. There are many medication choices, and no one treatment is right for every patient.

## WHEN TO REFER

As noted above, the diagnosis of OAB can be made empirically without the need for specialized evaluation, and treatment likewise can be initiated comfortably by the PCP. If initial treatment with behavioral therapy and medications fails to alleviate the symptoms, it is appropriate to refer the patient for consultation and advanced testing (Table 4), such as urodynamic studies.
The definition of “initial treatment” may vary among clinicians. Some may try only one medication, whereas others may be comfortable changing medications and titrating doses. Our view is that any medication should be given for 2 to 4 weeks before it is considered to have failed.

REFERENCES


Address: Matt T. Rosenberg, MD, Mid-Michigan Health Centers, 214 N. West Avenue, Jackson, MI 49201; matttoren@yahoo.com.