# *A practical primary care approach to overactive bladder*

Matt T. Rosenberg, MD,[1] Erik S. Witt,[1] Jack Barkin, MD,[2] Martin Miner, MD[3]

[1]Mid Michigan Health Centers, Jackson, Michigan, USA

[2]Department of Surgery, University of Toronto, Humber River Regional Hospital, Toronto, Ontario, Canada

[3]Departments of Family Medicine and Urology, Miriam Hospital, Brown University, Providence, Rhode Island, USA

ROSENBERG MT, WITT ES, BARKIN J, MINER M. A practical primary care approach to overactive bladder. *Can J Urol* 2014;21(Suppl 2):2-11.

*The evaluation and treatment of overactive bladder (OAB) starts in the primary care office and can be accomplished efficiently, effectively and, most importantly, safely. With appropriate knowledge of the disease and an understanding of what to look for the primary care physician (PCP) can readily make the empiric diagnosis and initiate treatment. The key for the PCP is to be able to distinguish the uncomplicated patient from the complicated one and know when to refer, if necessary. It is also essential to be able to able to identify confounding conditions that could either be the cause of the symptoms or, in fact, make them worse. The algorithm presented in this paper describes a simplified, yet complete, approach to the patient presenting with lower urinary tract symptoms (LUTS) consistent with OAB. In the paper, we explain the disease itself, its prevalence and impact, the evaluation as well as the different treatment modalities that are available for the patient. Appropriate follow up, therapy adherence techniques and referral recommendations are also discussed.*

**Key Words:** overactive bladder, primary care approach

## Introduction

The evaluation and treatment of overactive bladder (OAB) has often been considered the domain of the specialist, the urologist or urogynecologist, but not the primary care physician (PCP). One explanation may be historical as extensive testing was done in the initial work up. Another reason may be because the majority of PCPs have limited training in urologic disease, thus referral has been easier than delving into something outside of their comfort level. Recently, the American Urological Association (AUA) put out new guidelines describing a simplified approach advocating an evaluation that does not require testing in the uncomplicated case.[1] This truly does put the PCP in the position of the gatekeeper for OAB. Unfortunately, the PCP is spread very thin with a multitude of disease states to deal with as well as less and less time to spend with the patient. Add that to the limited urologic training and the result is an under-diagnosed and under-treated disease. However, OAB is not just a quality-of-life issue, there are also serious ramifications such increased fall and fracture risk, infections and skin breakdown from wet clothing. Education for the PCP is the key to assistance for the many that needlessly suffer from bladder issues. This education should clarify the simple approach necessary to identify the at-risk patient as well as present all of the therapeutic options. Most importantly, this education should show the PCP when it is appropriate to refer and the "red flags" to watch out for. It is for all of these reasons that we present a practical approach to the evaluation and treatment of OAB.

Address correspondence to Dr. Matt T. Rosenberg, Mid Michigan Health Centers, 214 N West Avenue, Jackson, MI 49201 USA

## Definition of disease

OAB is a syndrome or symptom complex defined as: "Urgency, with or without urgency incontinence, usually with frequency and nocturia.[2] Urgency is a sudden, compelling need to void which is difficult to defer. Frequency is defined as voiding more than 8 times per day. Nocturia is voiding more than once per night. Incontinence is defined as the involuntary loss of urine. It is referred to as urge incontinence (UI) when preceded by urgency and stress urinary incontinence (SUI) when this loss occurs while coughing, sneezing, laughing, or as a result of other physical activities.[3] These symptoms describe failure of the bladder to store urine, one of its basic functions. Another way to define bladder storage issues is to describe them as "irritative symptoms". This is a useful distinctive for the PCP when trying to differentiate those symptoms caused by bladder dysfunction, storage or irritative issues, from those symptoms caused by the prostate, obstructive or voiding issues. Obstructive symptoms describe difficulty with the act of voiding which include poor flow, hesitancy or intermittency. Obstructive symptoms are generally caused by the

enlarging prostate, which is commonly referred to as benign prostatic hyperplasia (BPH).[3] Combined, the symptoms arising from the bladder or the prostate are called LUTS or Lower Urinary Tract Symptoms.

## Prevalence

In a 2011 study in the United States Coyne et al demonstrated that the prevalence of OAB symptoms is greater than 30%. They found that 1 in 3 adults greater or equal to 40 years of age reported symptoms of OAB at least "sometimes". Although women appeared to have a higher prevalence from ages 40-70, after the age of 70 the levels were essentially the same.[4] To put this into perspective, patients suffer of OAB symptoms more commonly than diabetes, asthma, coronary artery disease or chronic sinusitis just to name a few.[5]

## Treatment gaps

Most patients wait long periods after symptom onset to seek treatment and many do not approach the PCP at all. Unfortunately many are embarrassed or are fearful that they will need invasive procedures or surgery. Some have the perception that there is a lack of available or effective treatment.[6] They alter their lifestyle and develop coping mechanisms such as using diapers or other absorbent products, wearing dark, baggy clothing, carrying extra sets of clothing or only traveling where they know bathrooms are readily accessible.[7] One study found that less than half of the patients with probable OAB discussed the symptoms with a PCP and it was the patient who generally initiated the conversation. Additionally, only a small percentage of eligible patients are prescribed medication.[8]

## Primary care approach

The key in the PCP approach to OAB is to be able to provide a simple evaluation as well as having effective and safe treatment options. This starts with acknowledging symptoms and then elucidating the cause. Treatment can be empiric once other urologic and non urologic causes of the LUTS symptoms are ruled out or dealt with. The algorithm presented here, Figure 1, offers a logical and practical approach in evaluating the patient with symptoms consistent with OAB.

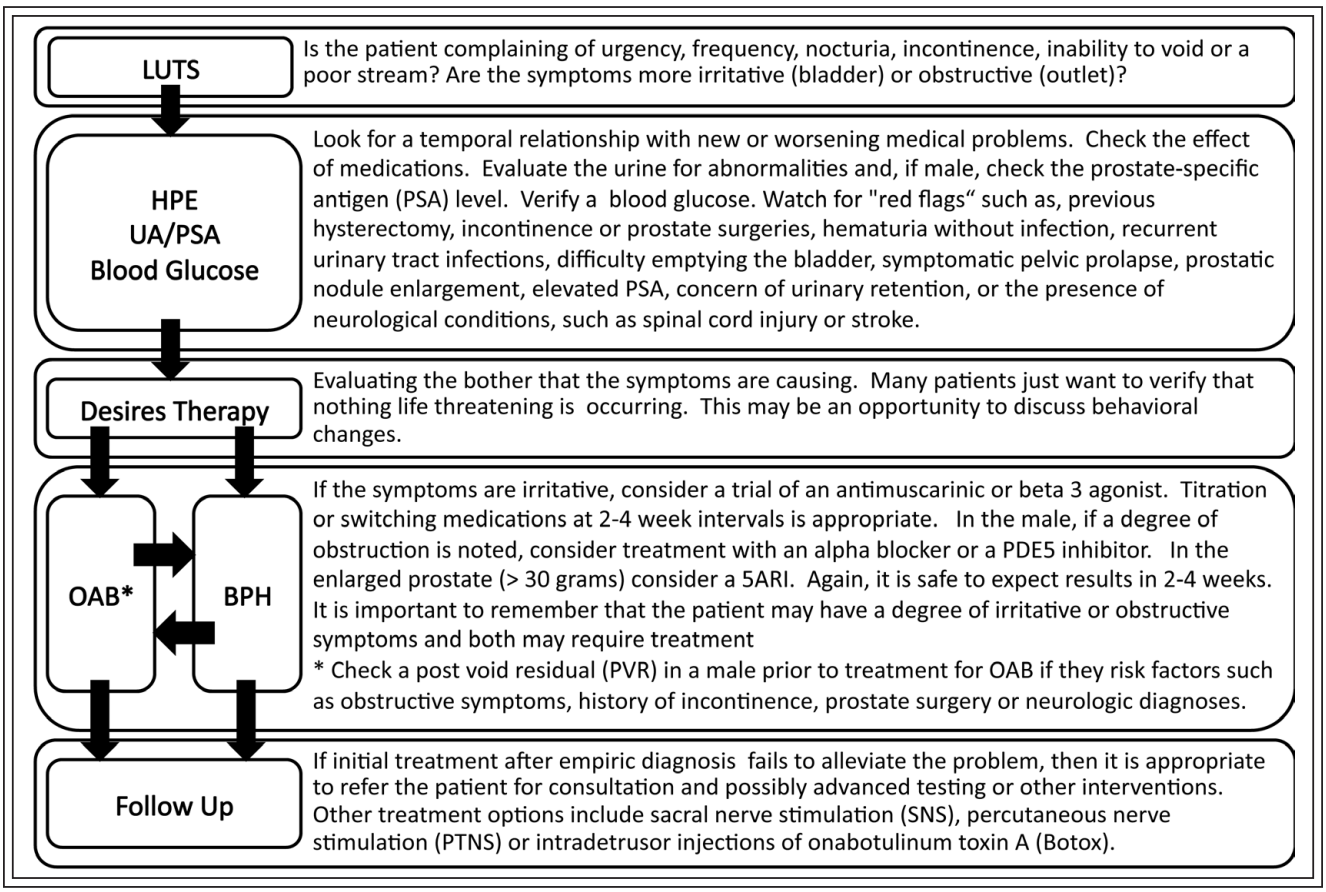


**Figure 1.** Practical approach in evaluating the patient with symptoms consistent with overactive bladder (OAB).

## Understanding symptoms

It is essential to recognize that symptoms consistent with OAB could be medically or urologically based. Therefore a good understanding of the function of the genitourinary organs (bladder and prostate) is crucial. In order to understand abnormal function of the urinary tract it is helpful to understand normal.

As mentioned earlier the bladder has the function urine storage. It must also void this urine when an adequate amount is attained. The bladder normally holds 300 mL-500 mL of fluid. It should be able to store this amount at a comfortable and low pressure. When 300 mL-500 mL is reached emptying should occur with an adequate and comfortable bladder contraction leaving a minimal residual. Abnormal function of the bladder is seen as voiding frequently of small amounts (frequency), having an uncontrollable urge (urgency), not having enough time or warning to reach the bathroom such that there is some leakage (urgency urinary incontinence), or incomplete emptying. Therefore, knowing the voided volume associated with the symptoms offers key insights into the bladder function and assists in identifying its role in the patient's symptoms. The bladder should also provide adequate outlet resistance. Decreased resistance results in incontinence.[3]

The normal function of the prostate is the production of fluid for seminal emission. As the male ages the prostate increases in size. By the sixth decade of life 50% of men will have some degree of prostate hyperplasia and by the eighth decade this will increase to 90%.[9] If this enlargement compresses the prostatic urethra then there is the possibility of obstruction of urinary flow as well as retention. The symptoms presented may include hesitancy, a weakened stream, intermittency or straining to void. Symptoms and bother depend on the degree of this obstruction. Therefore, knowing flow of urine offers key insights into the role of the prostate in the patient's problem.[10]

Understanding normal bladder or prostate activity subsequently helps the PCP understand when urinary function runs afoul. If the patient has any of the symptoms of urgency, urge incontinence, frequency, nocturia, hesitancy and/or decreased flow it is essential to try to elicit if the primary issue at hand is volume or flow. If it is volume, focus should be on the bladder. Volume per void can be readily attained with a bladder hat, or urine collection vehicle, that the patient can use in the privacy of their home. This would be kept in the form of a voiding diary that will be discussed in further detail later. If the primary problem is flow, then focus should be on obstruction which is generally the prostate in men, or maybe a prolapsed bladder in women.[3] Defining flow may seem difficult without a flow meter, but, in fact, adequate flow is exhibited with the "arc" of the void, not mL/sec. Most patients will understand an "arc" as opposed to a "dribble". If volume and flow are normal then the focus should be on why the patient has the enhanced fluid production which may be caused by a medical condition or a medication.

## Basic work up: identifying LUTS

The screening for OAB symptoms requires minimal time from a PCP as a self-administered screener or questionnaire can be used in most clinical settings. These tools are not meant to diagnose OAB or incontinence, rather to identify symptoms that may need treatment and to help rule out other significant or serious causes of LUTS.[3,11] Understandably, they may not always be practical in the office of the busy PCP in which case being familiar with the questions is helpful. Table 1 lists examples of questions regarding symptom onset, duration, severity and bother that may be useful.[3]

TABLE 1. **Simple screening questions for evaluation of overactive bladder and incontinence**

| | |
|---|---|
| Do you get sudden urges to go to the bathroom that are so strong you can't ignore them? | (OAB) |
| How often do you go to the bathroom? Is it more than 8 times in a 24-hour period? | (OAB) |
| Do you have uncontrollable urges to urinate that sometimes result in wetting accidents? | (urge incontinence) |
| Do you leak urine on the way to the bathroom? | (urge incontinence) |
| Do you frequently get up two or more times during the night to go to the bathroom? | (OAB) |
| Do you avoid places you think won't have a nearby restroom? | (OAB or urge incontinence) |
| When you're in an unfamiliar place, do you make sure you know where the restroom is? | (OAB or urge incontinence) |
| Do you leak urine when you laugh, cough or sneeze? | (stress incontinence) |
| Do you use absorbent pads to keep from wetting your clothes? | (stress incontinence or urge incontinence) |

## Basic work up: history, physical, labs and role of other tests

Once symptoms are identified the evaluation should turn to the history, physical and a limited laboratory evaluation. During the examination it is useful to pay attention to items that may be transient or reversible. It is also helpful to try to identify any temporal relationship between the patient's symptoms and any changes or new occurrences in their medical history. Recognizing the temporal relationship between the symptoms and recent medical conditions is helpful. The symptoms the patient has may well have been present for some time, however, a recent change (i.e., diet, surgery medication) may have exacerbated the problem.

The past medical history may identify poorly controlled diabetes, apnea, congestive heart failure or renal abnormalities. A full neurological history should be taken looking for the onset of dementia, Parkinson's, spinal cord injury or stenosis, multiple sclerosis or stroke. Functional and cognitive assessment should be performed on older adult patients. Dietary habits, especially fluids, have long been thought to be associated with urinary symptoms and should be addressed in the history.[3] Prior surgeries need to be addressed, especially any genitourinary intervention (examples include prostate surgery, 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 females as several or difficult vaginal deliveries can predispose the patient to OAB or stress incontinence. Medications should be reviewed to see if any association with the symptoms could be made. For example, the timing of a diuretic could have profound effects on urinary habits. Medications that can affect urinary function are listed in Table 2.[3]

TABLE 2. **Medications that affect bladder function**[3]

| **Medication** | **Effect** |
|---|---|
| Angiotensin converting enzyme inhibitors (captopril, lisinopril, enalapril) | Increased cough leading to stress urinary incontinence (UI) |
| Alpha-adrenergic agonists | Increase urethral resistance causing post void dribbling, straining, hesitancy in urine flow |
| Alpha-receptor agonists (pseudoephreine, ephedrine) | Urethral constriction, urinary retention (male) |
| Alpha-receptor antagonists (prazosin, terazosin, doxazocin) | Urethral relaxation and decreases urethral resistance causing stress UI (females) with UI with cough, sneeze, or other activity |
| Anticholinergics (H1 antihistamines, antiparkinsonian agents) | Urinary retention with symptoms of post void dribbling, straining, hesitancy in urine flow, overflow incontinence, fecal impaction |
| Antidepressants, tricyclic | Anticholinergic effect, alpha-receptor antagonist effect causing post void dribbling, straining, hesitancy in urine flow |
| Antipsychotics, sedatives | Act as sedative causing confusion, may relax destrusor muscle leading to urinary retention |
| Beta-receptor antagonists (propranolol, metoprolol, atenolol) | Urinary retention |
| Calcium channel blockers (verapamil, diltiazem, nifedipine) | Urinary retention, fecal impaction |
| Diuretics | Increases urine production (polyuria) and volume leading to urgency and frequency |
| Methylxanthines (caffeine, theophylline) | Polyuria, bladder irritation |
| Neuroleptics (thioridazine, chlorpromazine) | Anticholinergic effect, sedation |
| Other (caffeine and alcohol) | Act as diuretic leading to urgency and frequency, induces sedation |
| Opiods | Urinary retention, fecal impaction, sedation, delirium |
| Sedative-hypnotics | Sedation effect may relax detrusor muscle |

The physical examination should focus on detecting abnormalities that could contribute to the symptomology. The neurological examination could start by observing the patient's gait as they walk into the room or down the hall. Noting a limp, poor coordination, dysarthria, facial asymmetry or other findings may indicate neurological conditions such as a stroke or multiple sclerosis. A brief mental status examination can be performed by observing the patient's general appearance and their response to questions. Alertness, orientation, memory and thought content can be useful parameters in assessing the patient.

Body mass index (BMI) should be noted as there is a strong relationship between increasing BMI (> 30) and the likelihood of female UI.[11] Identifying this correlation provides an opportunity for the PCP to discuss lifestyle changes for the patient as moderately obese women who undergo even a small weight loss can decrease their LUTS.

The abdomen should be checked for masses, hernias or a distended bladder. In the female, the genitalia is assessed for vaginal abnormalities such as a prolapse of the bladder or uterus, atrophic vaginitis or urogenital atrophy and rectal sphincter tone. Having the patient cough during the pelvic exam may help identify SUI. In a male, it is important to assess the prostate for enlargement, nodules, asymmetry or tenderness. The penis should be examined for scars lesions or meatal stenosis. If a foreskin is present it should be checked to verify that it can retract over the glans and is not phimotic. The rectum should also be assessed for tone.

A urinalysis performed by dipstick or microscopic examination is strongly recommended to check for blood, protein, glucose or any signs of infection.

Although hematuria or pyuria are not always found in conditions such as bladder cancer, stones or infection, a normal urinalysis makes these diagnoses less likely.[1] It is not adequate to use the urinalysis to rule out the possibility of diabetes as the serum blood sugar must be over 180 mg/dL before glucose is spilled into the urine.[12] Therefore fasting or random blood sugar is needed to identify hyperglycemia as the onset of polyuria/polydipsia in the diabetic could certainly mimic the symptoms of OAB. If the PCP suspects obstruction in the male patient renal function studies may identify upper tract involvement.

There has been tremendous controversy regarding checking the prostate-specific antigen (PSA) level.[13] It must be remembered that the PSA is prostate specific and not cancer specific. In fact, it was shown that a PSA value of 1.5 ng/mL, in any age male, correlates to a minimal volume of 30 cc.[14] Knowing the size of the prostate can help guide therapeutic options. As was shown in the placebo arm of the Medical Therapy of Prostatic Symptoms (MTOPS) a prostate volume of 31 cc is directly related to increased risk of progression or worsening of LUTS caused by the obstructing prostate.[15]

A bladder or voiding diary can be very helpful in evaluating the extent of the problem and offering clues on how best to proceed with evaluation and treatment. It is a simple and practical method of obtaining detailed information about a patient's voiding habits.[7] The basic structure of the diary or log is to keep track of timing of the voided volume as well as preceding urgency. With the use of a diary patients may become aware of various habits that contribute to their symptoms that they can subsequently be changed in order to eliminate or minimize symptoms. For instance, they may find the problems are only at work when they may be rushing through the voiding process, when drinking a large amount of fluid at the movie or unable to readily access a restroom.

The post void residual (PVR) is not necessary in the initial evaluation of the uncomplicated patient (i.e., patients without a history of or risk factors for urinary retention).[1] Risk factors for retention include obstructive symptoms, history of incontinence, prostate surgery or neurologic diagnoses. Although there are many opinions regarding the absolute values, a PVR of less than 50 mL represents reasonably efficient voiding and therefore places the patient at low risk of retention. A PVR over 200 mL is consistent with clinically significant inadequate emptying and therefore the patient is at higher risk of retention.[12] An increased PVR may be a problem as it causes a significant decrease in functional bladder capacity which can lead to symptoms of urgency, frequency or nocturia.[16] A high PVR can also result in recurrent urinary tract infections.[17] In regards to the patient with BPH, a large residual urine volume is consistent with a significant risk of disease progression. One reason to check the PVR is when the patient's symptoms are refractory to initial therapy and the PCP is trying to check for retention as a result of severe obstruction as the source for the poor response. If this value is needed, it can be measured by direct catheterization or ultrasound scanning. Regardless of the technique used it is important for the patient to have the test performed when they have a full bladder.

Urodynamic studies are not necessary in the majority of patients, especially those without neurologic compromise, and are not recommended in the uncomplicated patient.[1] If the patient is refractory to therapy or symptoms worsen, then the test may be considered as one looks for other causes such as detrusor sphincter dysenergia. Cystoscopy has a role only in the

patient with hematuria or who is refractory to therapy. Radiological evaluation, beyond a portable bladder ultrasound, is reserved for those with hematuria or a palpable mass noted on examination.

## Red flags

Referral to a specialist should be considered if a significant finding is discovered during a work up. Criteria for referral include an uncertain diagnosis, unsuccessful therapy, previous surgery such as a hysterectomy, previous incontinence surgeries, hematuria without infection, recurrent urinary tract infections, difficulty emptying the bladder, symptomatic pelvic prolapse, prostatic nodule enlargement, abnormal PVR volume, or the presences of neurological conditions, such as spinal cord injury, stroke or an abnormal PSA, if tested.

## Treatment choices: is therapy wanted?

The PCP should recognize that not all patients desire intervention. They may have been concerned that the symptoms they presented with represent something life threatening. They may believe that taking medications or any other intervention is of greater concern than symptoms or even some of the associated quality-of-life issues.[18] One simple question at this point may be enough: "Are your symptoms bad enough that it would justify taking a medication each day or having a surgical procedure?" This should be asked in such a way that the patient is aware that they can come back at any time if, and when, they are ready for intervention. All patients, whether they choose intervention or not, may benefit from behavioral modifications. Behavioral modification involves educating the patient as to the normal process of micturition and then showing them how their specific symptoms define an abnormal situation. The goal of this intervention is to teach the patient to inhibit urgency and to improve voluntary control over bladder function. If the patient is actively involved in the diagnosis and then subsequent treatment, their expectations are more readily attainable. Behavioral therapy may involve pelvic floor muscle exercises, bladder retraining (which includes patient education and timed or delayed voiding), changing the timing of various medications like diuretics, dietary changes (i.e., reducing or eliminating the intake of caffeinated beverages) or encouraging exercise and weight loss. Preventing or alleviating constipation can also help avoid OAB symptoms.

This behavioral modification should be offered to all patients regardless of the chosen interventions. The literature shows that the combination of both behavioral and pharmacological therapies greatly enhances the likelihood of a positive outcome compared with either intervention alone.[19]

## Treatment choices: overactive bladder

*This is for the patient with identified irritative symptoms who desires therapy.*

The principle of pharmacologic management of OAB is to curb the symptoms. The most bothersome and most significant symptom of OAB is urgency with or without urgency incontinence. The patients will void frequently with small volumes. The goals of treatment are to decrease the urgency, increase the voided volumes and interval between voids. Therefore, medications to treat OAB should either block contraction of the bladder or facilitate storage. Although, many PCPs are apprehensive about treating men with OAB for the fear of causing retention the risk is, in fact, very low.[12] Currently there are two classes of medications to treat OAB, antimuscarinics which inhibit contraction of the bladder and beta 3 agonists that facilitate bladder relaxation.

The antimuscarinic class has been available for many years and there are several options, Table 3.[20] They are all efficacious in treating the symptoms of OAB within a few weeks, although titration of the medication or switching within the class may be necessary to achieve a suitable result for the patients. The side effects of dry mouth, constipation, headaches and blurred vision occur across the class, however, the degree for each agent varies and the extended release medications fare better in this regard than the immediate release. The contraindications for use of antimuscarinics include urinary or gastric retention as well as uncontrolled narrow-angle glaucoma. Warnings include angiodema (face, lips, tongue, and larynx), clinically significant bladder outlet obstruction and decreased gastric motility. There are precautions for CNS effects (especially in the elderly) as well as in use in patients with myasthenia gravis. There have been some recent studies, such as DuBeau et al (fesoterodine) that have demonstrated the safety and efficacy of certain OAB drugs in medically complex vulnerable elderly patients (mean age 75).[21]

The beta 3 agonist class is the new entry for the treatment of OAB. Currently there is only one medication available, mirabegron, Table 3.[20] The recommended starting dose of 25 mg is effective within 8 weeks. Based on patient efficacy and tolerability the dose may be increased to 50 mg anytime within that 8 week period. There are no contraindications listed

TABLE 3. **Medications for overactive bladder[20]**

| Drug | Brand name | Dose | Dosing | Indications |
|---|---|---|---|---|
| **Antimuscarinics - immediate release (IR)** | | | | |
| Oxybutynin IR | Ditropan | 5 mg | 2-4 x/day | OAB |
| Tolterodine IR | Detrol | 1 mg-2 mg | Twice daily | OAB |
| Trospium chloride | Sanctura (US)<br>Trosec (Canada) | 20 mg | Twice daily | OAB |
| **Antimuscarinics - extended release (ER)** | | | | |
| Darifenacin ER | Enablex | 7.5 mg, 15 mg | Daily | OAB |
| Fesoterodine ER | Toviaz | 4 mg, 8 mg | Daily | OAB |
| Oxybutynin ER | Ditropan XL | 5 mg-30 mg | Daily | OAB |
| Oxybutynin TDS | Oxytrol | 3.9 mg = 1 patch | Twice weekly | OAB |
| Oxybutynin 10% gel | Gelnique | 100 mg = 1 g of gel | Daily | OAB |
| Solifenacin | Vesicare | 5 mg, 10 mg | Daily | OAB |
| Tolterodine ER | Detrol LA | 2 mg-4mg | Daily | OAB |
| Trospium chloride | Sanctura XR (US) | 60 mg | Daily | OAB |
| **Beta 3 agonists** | | | | |
| Mirabegron | Myrbetriq | 25 mg, 50 mg | Daily | OAB |

in the prescribing information. Common side effects include hypertension, nasopharyngitis, urinary tract infections or headaches. It is not recommended for use in severe uncontrolled hypertension. It should be used with caution in patients with urinary retention or with bladder outlet obstruction or in patients taking an antimuscarinic.[20]

Although the antimuscarinic and beta 3 agonist class are the first line of pharmacologic therapy for OAB there may be a role for other medications. Estrogen therapy (transvaginal) also may have a role in treatment of the irritative symptoms of urgency and frequency associated with vaginal and urogenital atrophy; however, there is a lack of data which support any particular dosing regimen, route of administration, or treatment duration.[22]

## Treatment choices: prostate related LUTS (BPH)

*This should be considered for the symptomatic male patient with obstructive symptoms alone or mixed with irritative symptoms who desires therapy.*

OAB and BPH can certainly both occur in the male so the question becomes which to treat first. There is an understandable concern that the inhibitory effect of antimuscarinics and beta 3 agonists may worsen voiding difficulties or result in retention, especially in men at risk.[20,23,24] Although the risk is low, a logical and safe approach is to treat the obstructive symptoms first. Furthermore, there are data showing that treatment of the voiding component of LUTS can also improve the storage symptoms.[25] Then, if symptoms persist, the provider can add on or substitute treatment for the irritative symptoms.[26]

Initiating treatment with an alpha-blocker, or alpha antagonist, is an option for the obstructive patient with a small prostate (< 30 mL). The currently recommended medications include the non-selective second generation alpha-blockers (doxazosin and terazosin) and more uroselective third generation alpha-blockers (alfuzosin, tamsulosin, silodosin).[20] By inhibiting alpha1-adrenergic-mediated contraction of prostatic smooth muscle, alpha-blocker therapy relieves the bladder outlet obstruction with a noticeable effect for the patient within a few days.[1] For many men, this is sufficient for satisfactory relief of symptoms. Patients with smaller prostates tend to benefit the most from this monotherapy. Treatment failure with alpha-blockers is higher in men with larger prostate volumes.[27] Common side effects reported with alpha-blocker therapy include orthostatic hypotension, dizziness, tiredness, ejaculatory problems and nasal congestion.[1] The uroselective alpha-blockers seem to have fewer side effects than the non-selective ones; however, they can be associated with light-headedness and a higher incidence of ejaculatory dysfunction. An additional risk is floppy iris syndrome noted during cataract surgery.[28] As a result of this risk, ophthalmologists preparing the patient for cataract surgery should be aware of current alpha-blocker use. As a class, the alpha-blockers work quickly, with patients possibly noting a response within a few days.

The PDE5i class is relatively new as a treatment for BPH-LUTS. In the United States, Canada, Europe and some Asian countries only tadalafil is approved for this indication, although others have been studied.[29-33] The exact mechanism of action is unknown, it is believed that the PDE5i increase the signaling of the NO/cGMP pathway, which, in turn, reduces smooth muscle tone in the lower urinary tract.[34] In a study published in 2012, Oekle et al compared tadalafil and tamsulosin in a placebo controlled study. They noted statistically significant, yet similar, improvements versus placebo in BPH-LUTS as early as 1 week which was sustained for the 12 week study period. PDE5i differentiate themselves from alpha-blockers with the effect on sexual dysfunction. The most significant, yet expected, difference was that tadalafil improved erectile dysfunction.[35] Common side effects of the PDE5i include headache, back pain, dizziness and dyspepsia. These side effects are less in the once daily dosing used for BPH as opposed to the on-demand dosing used for erectile dysfunction.[36,37] They are contraindicated in patients who use nitrates, and should be used with caution in patients treated with alpha-blockers, since the combination may lead to hypotension. Tadalafil should not be used in patients with a history of non-arteritic anterior ischemic optic neuropathy (NAION).[20] Cardiac status must be assessed for patient risk before taking these medications.[38]

Patients with a large prostate (> 30 mL) may find that treating the dynamic component of BPH-LUTS with only an alpha-blocker or a PDE5i is not sufficient, and neither of those medications will halt the growth of the prostate. This enlargement may result in worsening symptoms as well as the risk of acute urinary retention and possibly the need for surgical intervention. The goal of therapy then becomes preventing the progression by reducing the static component or the bulk of this enlarged gland. Prostate growth is stimulated by dihydrotestosterone (DHT) with is converted from testosterone by the 5-alpha reductase inhibitor (5ARI). Decreases in DHT have been shown to induce prostatic epithelial apoptosis, reducing prostate size and decreasing PSA up to 50% after 6-12 months.[39-41]

There are two 5ARIs available, finasteride and dutasteride.[20] Both medications showed significant improvement over placebo in reducing prostate size and reducing the risks of symptom progression, acute urinary tract retention and surgical intervention.[41] Quick relief will not occur with the 5ARI alone as either medications generally require 3-6 months before the effect is noted. For this reason combination with an alpha-blocker or a PDE5i with the 5ARI is recommended. Studies have also shown that early and continued combination therapy results in significant improvement in symptom and bother scores as compared to monotherapy with either medication.[42-44] In regards to stopping combination therapy in favor of monotherapy, the studies are inconclusive and expert opinion favors continuing combination therapy in the at-risk patient.[10,45]

The most commonly reported adverse reactions of the 5ARIs include decreased libido, ejaculatory disorders, erectile dysfunction and gynecomastia.[20] The clinician should be aware that the PSA level will reduce approximately 50% within the first year and should never increase as long as the 5ARI is still be used. Any elevation should therefore be investigated.[1] Two crucial trials on prostate cancer chemoprevention found a slightly higher incidence of high-grade cancers in the 5ARI patients as compared to those taking placebo.[46,47] Although experts have debated the relationship the patient should be made aware of the risk and monitored appropriately.

## Follow up

There is no set rule on the interval for follow up after initiating treatment for OAB. Some PCPs find a 2 week interval is adequate while others recommend 4 week. What is important is that there is a conversation between the patient and the PCP outlining expectations. The PCP should address these expectations and encourage the patient not to give up if these expectations are not met immediately.[48] Each follow up appointment should reinforce behavioral modifications as well as medication compliance. If the initial medication dose does not provide the desired effect then a simple drug change or titration may help. There are many medication choices and no one treatment is right for every patient, therefore, failing with one drug or class allows an opportunity to try another. Historically, there has been a high discontinuation rate with OAB therapy. Having multiple medications within a class, as well as more than one class may assist in reversing this trend.

If a PVR was performed as part of the initial evaluation, it may be prudent to check it again during the follow up period. Studies have shown that if retention is to occur when on medication therapy, it is likely to happen within the first 30 days.[26]

## When to call in the specialist

As emphasized throughout this paper, the diagnosis of OAB can be made empirically without the use of specialized equipment or testing, and thus, treatment can be initiated comfortably by the PCP. However, it can be expected that in some cases treatment will fail to alleviate the problem even after switching medications or titrating them. In that situation it is appropriate to

refer the patient for consultation and possibly advanced testing or other interventions.

Other treatment options include sacral nerve stimulation (SNS), percutaneous nerve stimulation (PTNS) or intradetrusor injections of onabotulinum toxin A (Botox).[1]

## Conclusion

The evaluation and treatment of uncomplicated OAB should, most definitely, be in the domain of the PCP. However, facilitating this takes the teamwork of the patient, the PCP and the specialist. The patient must be willing to discuss his or her symptoms, make recommended lifestyle changes and adhere to prescribed medications. The PCP, must first ask the questions and then needs to educate the patient on normal versus abnormal urinary function, be able to diagnose OAB, set realistic goals, provide initial treatment and refer when necessary. In addition to offering treatment for the refractory or complicated patient, the specialist must offer education for the PCP in regards to initial management and, more importantly, what "red flags" to watch for and when to refer. OAB does not take your life, but it can steal it. Awareness can help those that suffer in silence.

## Disclosures

Dr Matt T. Rosenberg has been a speaker and consultant for Astellas, Easai, Ferring, Forest, Horizon, Ortho-McNeil, Lilly, Pfizer and Bayer. Erik S. Witt has no potential conflict of interest. Dr. Jack Barkin has been a clinical investigator, speaker and medical advisory board member and consultant for Abbott, Lilly, Bayer, Paladin, Actavis, AstraZeneca, Astellas, Pfizer and Triton. Dr. Martin Miner has been a consultant for Abbvie and Endo. He has also done research for Forest. □

References


1. Gormley EA, Lightner DJ, Burgio KL et al. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline. *J Urol* 2012;188(6 Suppl):2455-2463.
2. Wein AJ, Rovner ES. Definition and epidemiology of overactive bladder. *Urology* 2002;60(5-Suppl 1):7-12.
3. Rosenberg MT, Newman DK, Tallman CT et al. Overactive bladder: recognition requires vigilance for symptoms. *Cleve Clin J Med* 2007;74(Suppl 3):S21-S29.
4. Coyne KS, Sexton CC, Vats V et al. National community prevalence of overactive bladder in the United States stratified by sex and age. *Urology* 2011;77(5):1081-1087.
5. Stewart WF, Van Rooyen JB, Cundiff GW et al. Prevalence and burden of overactive bladder in the United States. *World J Urol* 2003;20(6):327-336.
6. Milsom I, Abrams P, Cardozo L et al. How widespread are the symptoms of an overactive bladder and how are they managed? A population-based prevalence study. *BJU Int* 2001;87(9):760-766.
7. Ricci JA, Baggish JS, Hunt TL et al. Coping strategies and health care-seeking behavior in a US national sample of adults with symptoms suggestive of overactive bladder. *Clin Ther* 2001;23(8):1245-1259.
8. Dmochowski RR, Newman DK. Impact of overactive bladder on women in the United States: results of a national survey. *Curr Med Res Opin* 2007;23(1):65-76.
9. McVary KT, Roehrborn CG, Avins AL et al. Update on AUA guideline on the management of benign prostatic hyperplasia. *J Urol* 2011;185(5):1793-1803.
10. Rosenberg MT, Staskin DR, Riley J et al. The evaluation and treatment of prostate-related LUTS in the primary care setting: the next STEP. *Curr Urol Rep* 2013;14(6):595-605.
11. Hannestad YS, Rortveit G, Daltveit AK et al. Are smoking and other lifestyle factors associated with female urinary incontinence? The Norwegian EPINCONT Study. *BJOG* 2003; 110(3):247-254.
12. Rosenberg MT, Staskin DR, Kaplan SA et al. A practical guide to the evaluation and treatment of male lower urinary tract symptoms in the primary care setting. *Int J Clin Pract* 2007;61(9): 1535-1546.
13. Rehsia S, Shayegan B. PSA implications and medical management of prostate cancer for the primary care physician. *Can J Urol* 2012;19(Suppl 1):28-35.
14. Roehrborn CG. The utility of serum prostatic-specific antigen in the management of men with benign prostatic hyperplasia. *Int J Impot Res* 2008;20(Suppl 3):S19-S26.
15. Crawford ED, Wilson SS, McConnell JD et al. Baseline factors as predictors of clinical progression of benign prostatic hyperplasia in men treated with placebo. *J Urol* 2006;175(4):1422-1427.
16. Kaplan SA, Wein AJ, Staskin DR et al. Urinary retention and post void residual urine in men: separating truth from tradition. *J Urol* 2008;180(1):47-54.
17. May M, Brookman-Amissah S, Hoschke B et al. Post-void residual urine as a predictor of urinary tract infection--is there a cutoff value in asymptomatic men? *J Urol* 2009;181(6):2540-2544.
18. Emberton M, Cornel EB, Bassi PF et al. Benign prostatic hyperplasia as a progressive disease: a guide to the risk factors and options for medical management. *Int J Clin Pract* 2008;62(7): 1076-1086.
19. Burgio KL, Locher JL, Goode PS. Combined behavioral and drug therapy for urge incontinence in older women. *J Am Geriatr Soc* 2000;48(4):370-374.
20. Physicians' Desk Reference. 66th ed. Montvale, NJ: Thomson PDR; 2014.
21. DuBeau CE, Kraus SR, Griebling TL et al. Effect of fesoterodine in vulnerable elderly subjects with urgency incontinence: a double-blind, placebo controlled trial. *J Urol* 2014;191(2):395-404.
22. Moehrer B, Hextall A, Jackson S. Oestrogens for urinary incontinence in women. *Cochrane Database Syst Rev* 2003;(2): CD001405.
23. Blake-James BT, Rashidian A, Ikeda Y et al. The role of anticholinergics in men with lower urinary tract symptoms suggestive of benign prostatic hyperplasia: a systematic review and meta-analysis. *BJU Int* 2007;99(1):85-96.
24. Martín-Merino E, García-Rodríguez LA, Massó-González EL et al. Do oral antimuscarinic drugs carry an increased risk of acute urinary retention? *J Urol* 2009;182(4):1442-1448.
25. Liao CH, Lin VC, Chung SD et al. Therapeutic effect of α-blockers and antimuscarinics in male lower urinary tract symptoms based on the International Prostate Symptom Score subscore ratio. *Int J Clin Pract* 2012;66(2):139-145.
26. Kaplan SA, Roehrborn CG, Abrams P et al. Antimuscarinics for treatment of storage lower urinary tract symptoms in men: a systematic review. *Int J Clin Pract* 2011;65(4):487-507.

27. Djavan B, Chapple C, Milani S et al. State of the art on the efficacy and tolerability of alpha1-adrenoceptor antagonists in patients with lower urinary tract symptoms suggestive of benign prostatic hyperplasia. *Urology* 2004;64(6):1081-1088.
28. Chang DF, Campbell JR. Intraoperative floppy iris syndrome associated with tamsulosin. *J Cataract Refract Surg* 2005;31(4): 664-673.
29. Roehrborn CG, McVary KT, Elion-Mboussa A et al. Tadalafil administered once daily for lower urinary tract symptoms secondary to benign prostatic hyperplasia: a dose finding study. *J Urol* 2008;180(4):1228-1234.
30. Mulhall JP, Guhring P, Parker M et al. Assessment of the impact of sildenafil citrate on lower urinary tract symptoms in men with erectile dysfunction. *J Sex Med* 2006;3(4):662-667.
31. McVary K, Monnig W, Camps JJ et al. Sildenafil citrate improves erectile function and urinary symptoms in men with erectile dysfunction and lower urinary tract symptoms associated with benign prostatic hyperplasia: a randomized, doubleblind trial. *J Urol* 2007;177(3):1071-1077.
32. Stief C, Porst H, Neuser D et al. A randomised, placebo-controlled study to assess the efficacy of twice-daily vardenafil in the treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia. *Eur Urol* 2008;53(6):1236-1244.
33. Gacci M, Vittori G, Tosi N et al. A randomized, placebo-controlled study to assess safety and efficacy of vardenafil 10 mg and tamsulosin 0.4 mg vs. tamsulosin 0.4 mg alonein the treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia. *J Sex Med* 2012;9(6):1624-1633.
34. Uckert S, Oelke M, Stief CG et al. Immunohistochemical distribution of cAMP- and cGMP-phosphodiesterase (PDE) isoenzymes in the human prostate. *Eur Urol* 2006;49(4):740-745.
35. Oelke M, Giulano F, Mirone V et al. Monotherapy with tadalafil or tamsulosin similarly improved lower urinary tract symptoms suggestive of benign prostatic hyperplasia in an international, randomized, parallel, placebo-controlled clinical trial. *Eur Urol* 2012;61(5):917-925.
36. Montorsi F, Verheyden B, Meuleman E et al. Long-term safety and tolerability of tadalafil in the treatment of erectile dysfunction. *Eur Urol* 2004;45(3):339-344; Discussion 344-345.
37. Porst H, Rajfer J, Casabé A et al. Long-term safety and efficacy of tadalafil 5 mg dosed once daily in men with erectile dysfunction. *J Sex Med* 2008;5(9):2160-2169.
38. Nehra A, Jackson G, Miner M et al. The Princeton III Consensus recommendations for the management of erectile dysfunction and cardiovascular disease. *Mayo Clin Proc* 2012;87(8):766-778.
39. Gittens PR, Lallas CD, Pe ML et al. Uropharmacology for the primary care physician. *Can J Urol* 2008;15(Suppl 1):78-91.
40. Rittmaster RS, Norman RW, Thomas LN et al. Evidence for atrophy and apoptosis in the prostates of men given finasteride. *J Clin Endocrinol Metab* 1996;81(2):814-819.
41. Naslund MJ, Miner M. A review of the clinical efficacy and safety of 5a-reductase inhibitors for the enlarged prostate. *Clin Ther* 2007;29(1):17-25.
42. Roehborn C, Siami P, Barkin J et al. The effects of combination therapy with dutasteride and tamsulosin on clinical outcomes in men with symptomatic benign prostatic hyperplasia: 4-year results from the combat study. *Eur Urol* 2010;57(1):123-131.
43. Kaplan SA, Roehrborn CG, McConnel JD et al. Long-term treatment with finasteride results in a clinically significant reduction in total prostate volume compared to placebo over the full range of baseline prostate sizes in men enrolled in the MTOPS trial. *J Urol* 2008;180(3):1030-1032.
44. Morlock R, Goodwin B, Gomez Rey G et al. Clinical progression, acute urinary retention, prostate-related surgeries, and costs in patients with benign prostatic hyperplasia taking early versus delayed combination 5α-reductase inhibitor therapy and α-blocker therapy: a retrospective analysis. *Clin Ther* 2013;35(5): 624-633.
45. Kaplan SA. Editorial comment on: effect of discontinuation of 5alpha-reductase inhibitors on prostate volume and symptoms in men with BPH: a prospective study. *Urology* 2009;73(4): 2417.
46. Andriole G, Bruchovsky N, Chung LW et al. Dihydrotestosterone and the prostate: the scientific rational for 5-alpha reductase inhibitors in the treatment of benign prostatic hyperplasia. *J Urol* 2004;172(4 Pt 1):1399-1403.
47. Thompson IM, Goodman PJ, Tangen CM et al. The influence of finasteride on the development of prostate cancer. *N Engl J Med* 2003;349(3):215-224.
48. DeCastro J, Stone B. Improving therapeutic outcomes in BPH through diagnosis, treatment and patient compliance. *Am J Med* 2008;121(8 Suppl 2):S27-S33.