doi: 10.1111/j.1742-1241.2007.01491.x

REVIEW ARTICLE

International Journal of Clinical Practice

A practical guide to the evaluation and treatment of male lower urinary tract symptoms in the primary care setting

M. T. Rosenberg,[1] D. R. Staskin,[2] S. A. Kaplan,[3] S. A. MacDiarmid,[4] D. K. Newman,[5] D. A. Ohl[6]

SUMMARY

Aims: Lower urinary tract symptoms (LUTS) are common in both men and women, and are among the most prevalent patient complaints heard by primary care physicians (PCPs). This article aims to provide PCPs with a logical algorithm for the assessment and initiation of treatment for LUTS in the male patient. **Results:** Management of LUTS involves a focused history and physical, as well as the assessment of bother. In patients for whom treatment is warranted, a series of decisions regarding therapy should be considered. Male patients commonly suffer from storage and/or voiding symptoms. Treatment of male LUTS is commonly begun with agents that are aimed at remedying the outlet symptoms of benign prostatic hyperplasia (BPH). When this intervention is ineffective or when refractory symptoms persist, consideration should be given to treating the storage symptoms characteristic of overactive bladder (OAB). **Discussion:** This article is intended to provide the PCP with a logical guide to the treatment of male LUTS. Benign prostatic hyperplasia and OAB predominate among the causes of these symptoms, and the PCP should be comfortable treating each. Recent data detailing the safety of the use of these treatments in the male patient are reviewed and incorporated into the algorithm. **Conclusion:** Primary care physicians are in a unique position to successfully identify and treat male patients with LUTS. With this paper, they now have a tool to approach treatment logically and practically.

Review Criteria

Male patients experiencing LUTS are likely to suffer from BPH. Recent evidence confirms, however, that these patients may solely or additionally suffer from OAB. Moreover, it has been shown that antimuscarinic therapy can be both effective and safe in these patients.

Message for the Clinic

Primary care physicians are provided with a simple and logical approach to treating LUTS in the male patient. This algorithm provides a guide that enables the PCP to effectively deduce the opportune points for treatment with multiple classes of drugs or referral to a specialist.

[1]Mid-Michigan Health Centers, Department of Family Medicine, Foote Health System, Jackson, MI, USA, President, Urologic Health Foundation
[2]Weill Medical College of Cornell University, Female Urology and Voiding Dysfunction, New York-Presbyterian Hospital, New York, NY, USA
[3]Institute of Bladder and Prostate Health, Weill Cornell Medical College, New York, NY, USA
[4]Bladder Control and Pelvic Pain Center, Greensboro, NC, USA
[5]Penn Center for Continence and Pelvic Health, Division of Urology, University of Pennsylvania Medical Center, Philadelphia, PA, USA
[6]Division of Andrology and Microsurgery, University of Michigan, Ann Arbor, MI, USA, Secretary/Treasurer, Urologic Health Foundation

Correspondence to:
Matt T. Rosenberg, MD,
214 N. West Avenue, Jackson, MI 49201, USA
Tel.: + 1 517 784 9189
Fax: + 1 517 784 9657
Email: matttoren@yahoo.com

Disclosures

The manuscript is not under consideration elsewhere and none of the manuscript's contents have been previously published. All authors have read and approved the manuscript. Dr Matt Rosenberg has received consulting fees from Astellas Pharma Inc., GlaxoSmithKline, Novartis Pharmaceuticals Corporation, Ortho-McNeil Pharmaceutical, Pfizer Inc., and Verathon Inc. He also has received fees from Esprit Pharma, Inc. and Ortho-McNeil Pharmaceutical for non-CME services, and he has conducted research on behalf of Sanofi-Aventis. Dr David Staskin has received intellectual property

Introduction

Two 52-year-old patients, one female and one male, in otherwise good health, presented with urinary urgency, frequency and nocturia. No physical or laboratory abnormalities were noted. The female patient was treated with an antimuscarinic for her presumed overactive bladder (OAB), while her male counterpart was prescribed an alpha blocker for his presumed benign prostatic hyperplasia (BPH). Why is it that these two patients, presenting with the exact same lower urinary tract symptoms (LUTS), would so commonly receive different initial therapies? Because obstruction is a highly unlikely cause of LUTS in the otherwise healthy female patient, OAB is a reasonable assumption. However, in the male patient, the initial empiric diagnosis of BPH may be correct, but the fact remains that not *all* cases of male LUTS equate to BPH.

It is only in recent years that urologists have begun acknowledging OAB as an independent cause of LUTS in males. It has taken time (for the trickle down) for primary care physicians (PCPs) to become similarly comfortable with recognising and safely treating OAB in the male patient. The evidence supports this shift in our understanding of LUTS in males. One study showed that 43% of older men with LUTS suffer from detrusor overactivity (DO), not bladder outlet obstruction (BOO) (1), and only 50% of men with preoperative DO will have resolution of DO after outlet reduction surgery (2). In another study, Kaplan et al. (3) showed that the majority of men under 50 years of age with LUTS do not, in fact, have BPH; their symptoms are likely attributable to another cause. Understanding this paradigm shift has important implications for patient care. Regardless of the underlying cause, if the patients' symptoms are not resolved as a result of prescribed therapy, they may suffer needlessly or even undergo unnecessary prostate surgery.

As the first to encounter these patients, the PCP is in a unique position to provide needed counselling

rights from or holds a patent with American Medical Systems. He has also received consulting fees and fees for non-CME services from Astellas Pharma Inc., Esprit Pharma, Inc. and Pfizer Inc. Dr Steven Kaplan has been a consultant for Allergan Inc., Astellas Pharma Inc., NeoTract Inc., Pfizer Inc. and Sanofi-Aventis. He has also participated in speakers' bureaus for GlaxoSmithKline, Pfizer Inc. and Sanofi-Aventis. Dr Scott MacDiarmid has participated in speakers' bureaus for Astellas Pharma Inc. and Novartis Pharmaceuticals Corporation. He has also participated in speakers' bureaus and has been a consultant for Esprit Pharma, Inc., Ortho-McNeil Pharmaceutical, Pfizer Inc. and Watson Pharmaceuticals, Inc. Diane Newman has received consulting fees from Astellas Pharma Inc., GlaxoSmithKline, Novartis Pharmaceuticals Corporation, Pfizer Inc., Sanofi-Aventis and Watson Pharmaceuticals, Inc. She has also performed contract research for Allergan Inc. and GTx, Inc. Dr Dana Ohl has received consulting fees from GlaxoSmithKline/Schering-Plough Corporation, Lilly and Pfizer Inc. He has also received fees from Auxilium Pharmaceuticals, GlaxoSmithKline, Lilly, Pfizer Inc. and Solvay Pharmaceuticals, Inc. for non-CME services. He has performed contract research for American Medical Systems and Bayer Pharmaceuticals Corporation, and has participated in a speakers' bureau for Lilly. He has indicated that he holds ownership interest (in the form of stocks, stock options or other ownership interest excluding diversified mutual funds) in SD Science.

and intervention (4). Doing so appropriately, however, requires that we look beyond the current dogma that LUTS in the male equates to BPH. The purpose of this paper is to present a new algorithm for the evaluation and management of male LUTS for the PCP.

Clinical definitions

Definition of LUTS

According to the International Continence Society (ICS), LUTS can be divided into storage symptoms, voiding symptoms and symptoms experienced postmicturition (Table 1) (5). As is evident from the table, storage symptoms tend to be irritative in nature, whereas voiding symptoms have a more obstructive cause.

Interestingly, LUTS in the male are usually attributed to BPH. As a result of this preset notion, men with LUTS are predominantly treated with alpha-adrenergic medications. Alternatively, LUTS in the female are predominantly attributed to OAB, and are thus treated with anticholinergic medications. To provide optimal care, PCPs must consider the full spectrum of conditions that can result in LUTS in every patient.

Definition of BPH

The term 'BPH' can be difficult for the provider, as it carries several interpretations and has become idiomatic over the years for a 'troublesome prostate.' In reality, BPH is the most likely, but not the only, condition from which male patients may experience LUTS. There are also subtle differences in accepted terminology that should be reviewed. The term 'BPH,' in fact, refers to the asymptomatic microscopic detection of prostatic hyperplasia, the benign proliferation of the prostatic stroma and epithelium. The palpable enlargement of the prostate gland, which can be diagnosed with clinical or ultrasound examinations, is called benign prostatic enlargement. Enlargement of the prostate that is accompanied by LUTS, when prostatic hyperplasia affects urinary flow, is referred to as benign prostatic obstruction (6,7). For the PCP, these differences in terminology are important to know when evaluating the literature, but are largely irrelevant in clinical practice. Therefore, for the sake of clarity, the authors will use the term 'BPH' to refer to the complex of symptoms experienced as a result of the troublesome prostate.

Definition of OAB

Overactive bladder is defined by the ICS as a syndrome including urinary urgency (the intense, sudden desire to void) with or without incontinence, urinary frequency (voiding too often during the day) and nocturia (awakening at night to void) (8,9). The symptoms of OAB are present in the absence of any pathologic or metabolic disorders that might otherwise result in symptoms. Together, BPH and OAB result in the overwhelming majority of cases of male patients with LUTS that present PCPs.

Pathophysiology

Lower urinary tract symptoms has a varied pathophysiology that may be multifactorial. While OAB is a symptom complex generally of unknown aetiology (with numerous theories), the voiding symptoms of BPH are presumably caused by prostatic enlargement that interferes with urinary flow. The aetiology of storage symptoms of BPH, however, remains controversial.

Pathophysiology of OAB

To understand the abnormal function suffered by the patient with OAB, it is instructive to start with normal bladder function. Micturition involves two important, yet discrete processes: (i) bladder filling and storage and (ii) bladder emptying (10). Normal bladder capacity is 300–400 ml of urine (9).

Table 1 Lower urinary tract symptoms

Storage symptoms	Voiding symptoms	Postmicturition
Frequency	Slow stream	Feeling of incomplete emptying
Nocturia	Splitting or spraying	Postmicturition dribble
Urgency	Intermittent stream	
Urinary incontinence	Hesitancy	
Stress incontinence	Straining	
Urge incontinence		

Adapted from Ref. (5).

Normally, adults first experience the urge to void before capacity reaches 200 ml (9,11). Second urge occurs later, at near-normal capacity, and the non-affected patient can generally hold off micturition for a reasonable amount of time to reach an appropriate facility. The filling and storage phase requires accommodation of increasing pressures with appropriate sensation, a closed bladder outlet and absence of involuntary contraction. For the bladder to empty, there must be a co-ordinated contraction of the bladder muscle, a lowering of the resistance of the outlet, and an absence of anatomic obstruction. Any type of voiding dysfunction can be classified by an abnormality of any one or more of these three factors.

The aetiology of OAB is heterogeneous, but the commonality is the inability to accommodate the increasing volumes of urine, with the increased sensation causing symptoms of urgency and frequency with or without a contraction. The urgency associated with OAB is defined as sudden, intense and difficult to deter. This is different from the normal urge sensation that still offers adequate time to prepare for voluntary micturition. Storage symptoms may result from abnormal signalling, a sensory amplification (afferent) or increased motor output (efferent).

Pathophysiology of BPH

The hyperplastic prostate, as a result of its close proximity to the urethra, can affect urinary flow by obstructing the urethra. This leads to the classic voiding symptoms associated with BPH: reduced stream and intermittency. Prostate enlargement, however, can also lead to overactivity of the detrusor muscle. It is unclear to what extent prostatic hyperplasia and obstruction incur storage symptoms (12).

Relationship of BPH and OAB

Figure 1 addresses LUTS and its relationship with BPH and OAB. OAB will always cause LUTS (by definition); BPH will sometimes cause LUTS. The two can also co-exist. Figure 1 graphically represents the relationship of OAB and BPH in the context of LUTS.

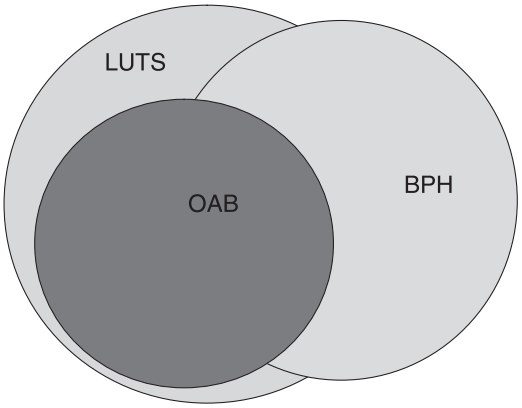

Figure 1 The relationship between overactive bladder (OAB) and benign prostatic hyperplasia (BPH) in the context of lower urinary tract symptoms (LUTS)

Impact (incidence/prevalence, quality of life, social implications)

As a result of high prevalence, the PCP is extremely likely to encounter LUTS among adult male patients. Stewart et al. (13), as part of the National Overactive BLadder Evaluation Programme, a large-scale epidemiologic survey of community-based adults over the age of 18, demonstrated that OAB occurs in 16–17% of Americans. Not surprisingly, the prevalence of OAB with urge incontinence increased with age. Perhaps less expected, however, was the fact that men were as likely to suffer from OAB as women, although women were more likely to report incontinence as a symptom.

Microscopic BPH affects approximately 50% of men 50–60 years of age (14), 75% of men 60–69 years of age and up to 90% of men over the age of 80 (15). This suggests that, in the USA alone, as an example, some 25 million men have a hyperplastic prostate (16). However, we have established that having a hyperplastic prostate does not equate to experiencing symptoms. It has been estimated that 9 million American men are affected by bothersome symptoms resulting from BPH (17).

For each of these increasingly prevalent conditions, the impact on the patient is substantial. LUTS can significantly reduce quality of life (18,19). Patients may resort to social isolation, become depressed, have reductions in productivity, experience poor sleep and often have an impaired sex life. LUTS is associated with the development of sexual dysfunction and ejaculatory problems, but impaired sex life can also be a result of the psychological implications of LUTS (9,19).

Furthermore, LUTS have significant economic implications. Direct costs associated with diagnosis and treatment make up the majority of this economic burden, but indirect costs can also be significant. Indirect costs include incidence of absenteeism (missing work) and presenteeism (decreased productivity at work). The estimated direct cost alone of BPH in males in the USA is $1.1 billion (15). Moreover, the pharmacologic treatment of LUTS, no

matter the underlying cause, has been shown to be economically cost effective (20,21).

Clinical presentation – using the algorithm

Differential diagnosis and other causes of LUTS

The utilisation of the clinical algorithm (Figure 2) proposed in this paper begins with differential diagnosis, ruling out other causes that require medical attention, and identifying contributing and/or precipitating factors. LUTS are not specific to any one entity and many urologic and non-urologic conditions can cause LUTS. Table 2 shows diagnoses in addition to BPH and OAB that the clinician must consider, medications that can cause or exacerbate urinary symptoms, and other risk factors for the development of LUTS.

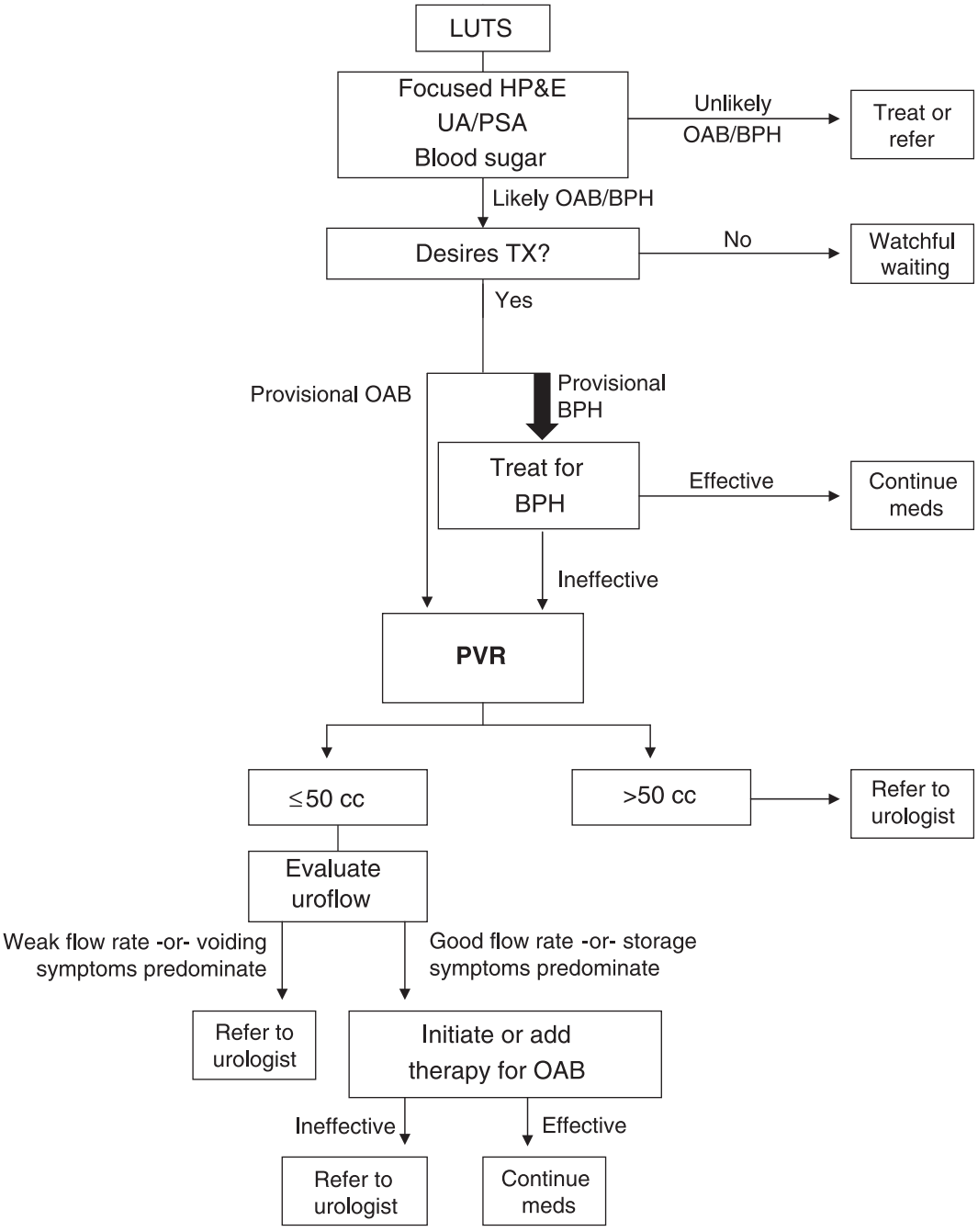

Figure 2 Clinical algorithm for the assessment and initiation of treatment of male lower urinary tract symptoms (LUTS)

Table 2 Lower urinary tract symptoms (LUTS): differential diagnosis and other causes (22,23)

Differential diagnosis	Medications	Other risk factors
Consider:	May cause or exacerbate LUTS:	Consider:
Bladder cancer	Tricyclic antidepressants	Obesity
Prostate cancer	Anticholinergic agents	Cigarette smoking
Prostatitis	Diuretics	Regular alcohol consumption
Bladder stones	Narcotics	Elevated blood pressure
Interstitial cystitis	First-generation antihistamines	
Radiation cystitis	Decongestants	
Urinary tract infection		
Diabetes mellitus		
Parkinson's disease		
Primary bladder neck hypertrophy		
CHF		
Lumbosacral disc disease		
Multiple sclerosis		
Nocturnal polyuria		

CHF, congestive heart failure.

It is essential that the provider keep the differential diagnosis for LUTS in mind during the evaluation of the patient. Certainly, OAB and BPH are common, but one should avoid making a premature judgment. In the following section, we analyse the algorithm for evaluation and treatment of LUTS in the male patient. One proceeds with the algorithm only if no other pathologies that could result in LUTS are identified.

Evaluation

The algorithm presented is designed for the PCP who is generally the first point of contact for the male patient with LUTS. It is not meant to address all possible contingencies, but rather to provide a logical framework from which one can initiate therapy or know when to refer. The authors believe that LUTS in men can be treated in the primary care setting; the algorithm provides a basis and direction for this practice to occur.

Identifying LUTS

The first challenge is to identify LUTS. This could possibly be the most difficult part of the evaluation, as patients can be quite reticent to proactively bring up these symptoms. Patients are likely to be embarrassed, believe that their symptoms are a normal part of ageing, or even fear surgery. Screening tools exist to help evaluate LUTS, however they may not always be practical in a busy primary care setting. In one study, it was shown that 2/3 of PCPs were aware of the American Urological Association (AUA) symptom score, but only 1/3 used it (4). Another screening tool, the International Prostate Symptom Scoring (IPSS) sheet, does have the advantage that it is universal and has been validated. Because other conditions can produce similar symptoms, however, it cannot be used as a diagnostic tool (24). The IPSS ideally would be used by all clinicians at this juncture, but, as an alternative, a few simple questions can also direct the physician to the disease.

History, physical and laboratory evaluation

Once LUTS have been identified, it is necessary to proceed with a focused history and physical, as well as a few laboratory tests. The goal of this evaluation is to identify other causes of the LUTS, possible reversible issues or comorbidities that may complicate treatment. The PCP has a distinct advantage over the specialist of having prior knowledge of the patient, making the information needed for the history readily available. For example, first-hand knowledge of recent changes in medications, family history or prior surgeries may expedite identifying a cause of LUTS.

A key to the proper evaluation of LUTS is to give special attention to the voiding volume that the patient produces. If the patient voids small amounts of urine frequently, then the urologic function is more likely to be abnormal. However, if the patient voids normal amounts frequently, then a medical cause is more likely than a urologic cause. Nocturnal polyuria, which is a potential cause of nocturia, is a good example of this concept. The definition of nocturnal polyuria is when more than 20% (in 'young adults') or more than 33% (in those older than

65 years) of a person's total 24-h urine production occurs at night (25). This is neither a storage nor a voiding symptom, because the bladder is behaving normally by holding and emptying a normal capacity of urine.

The physical examination should likewise be focused. One first conducts an abdominal examination to evaluate for tenderness, masses or an overdistended bladder, followed by a brief, focused neurological examination to check for patient's mental and ambulatory status and neuromuscular function. Next, the provider should conduct a thorough examination of the genitalia, including the meatus and testes. A digital rectal examination to evaluate rectal tone and prostate size, shape and consistency will provide the opportunity to detect prostatic implications in symptoms (24). Much of the physical examination may have been done at prior visits with the PCP, so that re-examination (i.e. prostate exam) may not be necessary. Again, one of the benefits to the PCP is that the patient's medical information and baseline physical examination is usually known.

A urinalysis performed by dipstick or microscopic examination is strongly recommended to check for blood, protein, glucose or any signs of infection. This may prompt treatment or referral (26). Although haematuria or pyuria is not always found in conditions such as bladder cancer, stones or infection, a normal urinalysis makes these diagnoses less likely (26). A prostate-specific antigen (PSA) measurement should be offered to age-appropriate males and referral made if abnormalities are found. Although not part of the AUA guidelines, there is a good argument for testing blood sugar, either random or fasting. Generally, a patient does not spill glucose into the urine until the blood sugar is > 180 mg/dl (10 mmol/l). Consequently, a dipstick urinalysis may fail to pick up on intermittently high sugars or mild diabetics (26). Urine cytology is optional, but may be performed prior to referral for evaluation of haematuria and may be considered in men with storage symptoms or at risk for bladder cancer (26). Although once recommended, serum creatinine is no longer indicated (26).

Any abnormalities found during the history, physical or laboratory evaluation that could possibly contribute to LUTS should be addressed by the clinician or referred to a urologist. Table 3 lists reasons for referral at this juncture. If none of these abnormalities are identified, it is appropriate to proceed with assessment of bother.

Table 3 Indications for referral

History of recurrent urinary tract infections or other infection
Microscopic or gross haematuria
Prior genitourinary surgery
Elevated prostate-specific antigen
Abnormal prostate exam (nodules)
Suspicion of neurologic cause of symptoms
Findings or suspicion of urinary retention
Meatal stenosis
History of genitourinary trauma
Uncertain diagnosis
Pelvic pain

Assessing bother

If the evaluation thus far reveals no other aetiology for the LUTS, the next step is to assess bother. As mentioned earlier, there are tools to assist in assessment of symptoms and bother. It is acknowledged that the validated scores (IPSS or AUA symptom index) are superior to an unstructured interview in quantifying symptom frequency and severity (26). Nevertheless, the practicality of these items in the primary care office can be questioned. Perhaps more importantly, a few simple yet pertinent questions can expedite care. This assessment should be left to the discretion of the provider. One of the authors (MTR) finds one simple question can be enough: 'Are your symptoms bad enough that they would justify taking a medication each day or having a surgical procedure?' In the clinical opinion of this author, most patients will answer honestly and appreciate being part of the process. A similar question from the validated IPSS scale (27) measures quality of life as it is affected by BPH: 'If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?'.

If assessment, by whatever means, reveals minimal bother then watchful and informed waiting is appropriate. 'Informed waiting' refers to the idea that the patient is knowledgeable of the symptoms or complications that may occur. If assessment leads to a decision to proceed with treatment, the clinician must then assess whether symptoms result from OAB or BPH. It should be noted that an assessment for haematuria, recurrent urinary tract infection (UTI), elevated PSA, neurological conditions and retention should be initiated based on risk irrespective of LUTS.

Is it OAB or BPH?

When dealing with the clinical presentation of LUTS, the clinician must first differentiate between storage and voiding issues, which were summarised earlier in Table 1. The reality is the provider cannot make a definitive diagnosis of obstruction without advanced

testing, such as urodynamics. This algorithm recommends making a provisional diagnosis using clinical judgment and a consideration of safety. We know that storage issues affect the bladder and the ability to hold urine, whereas voiding issues relate to obstruction and urine expulsion. If voiding symptoms such as poor flow or intermittency exist, then an obstructive cause is more likely the problem, and the focus is placed on the prostate. However, if storage seems to be the issue (as seen in urgency, frequency, etc.), one may consider OAB as a diagnosis. Of course, it is important to note that many patients exhibit both OAB and BPH, which must be considered when evaluating the path one takes through the algorithm.

Provisional BPH: behavioural and pharmacological therapy

As we proceed with the algorithm, the reader will notice that the arrow to the provisional diagnosis of BPH is larger than that to OAB. There are many reasons for this. The most important is that the authors believe that this clinical path is the most practical for the PCP, as minimal testing is required. It also follows typical practice patterns (4,28). Furthermore, an enlarged prostate may be the cause leading to the OAB. While there are tests that may aid in the decision-making process, such as pressure-flow studies and postvoiding residual (PVR) urine measurement, the recent AUA guidelines state that these are not necessary prior to the institution of medical therapy (26). Empiric medical therapy is appropriate at this juncture, but the provider must also consider the benefits of behavioural modification.

Behavioural modification can take several forms. Some patients benefit from improving access to the bathroom or a toilet. Some find assistance with decreased fluid intake. Diet can also play a role. One study suggested that increased intake of high energy foods (foods containing a large amount of caffeine) and protein may be a risk factor for BPH (29). Alternatively, another study found that a diet rich in vegetables and beta carotene, lutein and vitamin C may reduce the occurrence of BPH (30). Although dietary counselling may be outside the PCP's specialty, it is important to know that some data on this topic do exist, especially considering that patients are likely to find information about this in the lay press.

The medication armamentarium for the PCP in the treatment of BPH consists of alpha blockers and 5-alpha reductase inhibitors (5ARIs). Although there are other therapeutic modalities such as phytotherapy, they will not be discussed here.

Alpha blockers treat the 'dynamic' component of BPH, offering fast relief of symptoms (31). The mechanism is to inhibit activation of $alpha_1$ adrenergic receptors, which results in relaxation of prostatic and bladder neck smooth muscle and thus decreases LUTS (32). Frequently prescribed alpha blockers are alfuzosin, doxazosin, tamsulosin and terazosin. All four agents have comparable efficacy (26). Alfuzosin and tamsulosin are clinically uroselective, thereby resulting in fewer cardiovascular effects (i.e. vasodilatory adverse events) (33). Some patients may have specific comorbidities or characteristics that would lead to choosing one alpha blocker over another. For example, as a significant number of elderly men have hypertension, these men may derive benefit from a mixed subtype alpha blocker such as doxazosin or terazosin, both of which have been shown to reduce blood pressure levels in hypertensive men without affecting blood pressure levels in normotensive men (34,35). It should be noted, however, that using doxazosin or terazosin for this type of dual treatment has gone out of favour because of the advent of newer antihypertensive medications.

Five-alpha reductase inhibitors act on the 'static' component of the prostate by inhibiting the conversion of testosterone to dihydrotestosterone, thereby limiting prostate growth. The two medications in this class are finasteride and dutasteride. Both are effective when used in the patient with LUTS that are associated with demonstrable prostate enlargement (26). In particular, both have been noted to reduce the risk of acute urinary retention and the need for prostate surgery (36). The disadvantage of these agents is that they require long-term daily therapy (up to 6 months) before symptom relief is achieved (26). Moreover, the use of these agents can be complicated for the PCP, as these agents lower the serum PSA and, thereby, change screening parameters.

At this point in the algorithm, patient bother has been identified and most physicians believe that it is best to initiate therapy with an alpha blocker as opposed to a 5ARI, as these medications are most likely to provide immediate response. If successful, symptom resolution with alpha blocker therapy should occur within 2–4 weeks. If so, then periodic follow-up is all that is necessary. If the patient is adherent to the prescribed regimen, but it falls short of anticipated goals, one is left with the opportunity to use a 5ARI or to shift diagnosis. If the alpha blocker has provided some relief and the prostate is palpably enlarged, it is reasonable to try prostatic reduction via the 5ARI (26). It has been noted that men with bothersome LUTS and an enlarged prostate (> 30 ml) or a PSA > 1.4 ng/ml have an increased risk of complications such as acute urinary retention. Studies have shown that initiating dual therapy with an alpha blocker and a 5ARI may be advantageous in

these patients (24,37). It is critical, however, for the patient and the physician to accept this as a 'long-term' plan as response to 5ARI therapy may take up to 6 months and will need to be continued.

An important point to consider is that the alpha blocker may not have actually failed in relieving obstruction. It is also plausible that the most bothersome symptoms may be a result of storage complications (i.e. OAB) and, as such, this therapy was either not appropriate or did not provide complete relief. OAB symptoms may be exacerbated by BOO that results from BPH (38). Alternatively, if the alpha blocker fails to reduce LUTS at all, then additional diagnosis such as OAB should be considered. In general, men report that these medications do improve urinary flow and nocturia, but not urgency or frequency. In either of these scenarios, or any time OAB is considered, the algorithm recommends assessing the PVR. If this cannot be performed in the office of the PCP, the patient may be better served by referral to a urologist or other facility that can evaluate PVR (i.e. outpatient diagnostic center).

Provisional OAB

If the symptoms identified in the initial patient evaluation are more consistent with storage than voiding, the provisional diagnosis of OAB can be made. Similarly, if treatment for BPH proves ineffective, one can move to the OAB section of the algorithm to either shift diagnosis or add treatment for OAB. Unfortunately, with the treatment of OAB comes the possibility of placing a patient at risk of, or worsening a condition of, retention. In fact, the package insert for every antimuscarinic includes a warning that these agents should be used with caution in patients with BOO, and that they are contraindicated in patients with urinary retention. The terms 'retaining urine' and 'retention of urine,' and 'BOO' and 'urinary obstruction' have not been quantified. The dictum that anticholinergics in the male are to be 'utilised with caution' or are 'contraindicated' does not specify the amount of residual urine or the degree of outlet resistance that would put a patient at risk of further deterioration of clinically significant problems with bladder emptying. The evidence either way is lacking, and further studies will need to be performed to elicit the truth. However, it is this concern that leads to the recommendation of PVR assessment when considering treatment for OAB.

Measuring PVR

The measurement of PVR has been uniformly recommended in the literature as a useful screening tool for the male patient with LUTS (12,24,26), although these recommendations fall short of mandating its use. There may be many reasons for this. First, it is known that intra- and interindividual variability exists (24,39). Furthermore, as is the case for flow-rate testing, measurement of PVR does not distinguish obstruction from underactive bladder, nor does it correlate with urodynamic evidence of the severity or duration of obstruction (39). Even though large PVR volume may indicate bladder dysfunction and herald progression of disease, clear-cut parameters for decision making, as yet, do not exist (26). The AUA guidelines note that many patients maintain a significant PVR volume without evidence of UTI, renal insufficiency or bothersome symptoms. It is concluded, therefore, that no level of residual urine mandates invasive therapy.

Keeping all of this in mind, what does this mean for the PCP, and does the use of PVR measurement help? The algorithm notes that the goal at this juncture is to attempt to delineate the cause of LUTS; that is, whether the patient suffers from obstruction or from OAB. The obvious concern to the PCP is the possibility of missing the patient who is in retention or predisposed to it. To better account for these possibilities, the authors advocate the use of PVR. This may increase the comfort level of the PCP and thereby facilitate care. A clinically reasonable approximation of PVR can be made via transabdominal ultrasonography, portable bladder scanner or urethral catheterisation. Although there may be some variability in the precision data for portable bladder scanners (40), studies have confirmed their clinical accuracy (41,42), and they are more than adequate for the purpose of instituting therapy. In fact, a recent study found that a three-dimensional handheld scanner measured bladder volume more accurately than by using two-dimensional stationary ultrasonography (43). Bladder scanners are routinely used by urologists and acute care hospitals to determine bladder volume, and they provide a reasonable option for the office-based PCP. We propose a logical approach to using PVR to assist the PCP in the evaluation and treatment of LUTS.

PVR $\leq$ 50 ml

It is reasonable to believe that the patient with a minimal volume noted on PVR is at decreased risk for retention. We must then define minimal volume for the purposes of this algorithm. A review of the literature offers only limited help in defining this value, suggesting that further research on this topic is needed.

McNeill et al. (39) examined the correlation between PVR and clinical efficacy of an alpha blocker. In 953 patients followed, only seven went into retention during the study, two in the medication group

(0.3%) and five (1.3%) in the placebo group. Six of the seven that went into retention had a baseline PVR of > 100 ml. In the Olmsted County study (40), it was found that a PVR of > 50 ml at baseline resulted in a threefold increase in the risk for urinary retention. It is the opinion of the authors that the more conservative, and subsequently safer, PVR of ≤ 50 ml puts the patient at minimal risk for retention and should be utilised by the PCP. If the PVR is noted to be ≤ 50 ml, then the next step would to be to consider urinary flow (uroflow), which will be discussed in the following section.

PVR > 50 ml

It is conceivable that some PCPs may wish to adopt a higher cut-off value for the treatment of LUTS than the ≤ 50 ml recommended in this algorithm (9). This is not unreasonable given the findings by McNeill et al. (39) and the comfort level that some PCPs have with LUTS, BPH and OAB. Nevertheless, for PCPs who lack this experience or the comfort to treat these patients, it is the recommendation of the authors that patients with a PVR > 50 ml be referred to a specialist. One author (DN) recommends that if the PVR is elevated, the PCP may want to repeat the PVR at another visit to verify its validity.

Evaluating uroflow

In patients for whom the PVR is ≤ 50 ml, the next step is to evaluate uroflow. The benefit of uroflow testing in LUTS is not necessarily to point to BPH as a cause, but rather to exclude it as a diagnosis. One cannot say that a poor flow correlates with obstruction as this can also be caused by inadequate detrusor function. Nevertheless, it is reasonable to conclude that in a male with good flow the diagnosis of obstruction is unlikely (24).

Attaining a uroflow in the office of the PCP may be difficult and impractical. In a perfect world, every PCP would have access to a monitoring device; however, this is obviously not the case. It is the opinion of the authors that most men can give a fairly accurate self-evaluation of stream and that this often will suffice. To assist patients with the self-evaluations of their own urinary flow, the PCP can use helpful terminology, such as 'weak' or 'slow stream,' 'interruption of stream,' 'hesitancy in starting stream' or 'dribbling'.

Weak flow rate

Studies suggest that a very low flow rate (< 8 ml/s) is highly predictive of BOO (44). It is the opinion of the authors that such cases should be referred to a urologist.

Good flow rate

A good flow effectively reduces the likelihood of obstruction as a diagnosis and should place the focus of the provider on storage issues (bladder dysfunction). It is at this point that one should consider the diagnosis of OAB as the cause of the LUTS. It is difficult to offer an absolute measurement for 'good flow,' which can be defined as a smooth, arc-shaped curve with high amplitude as seen with uroflowmetry. As opposed to a weak flow, which would be interrupted, a good flow would not be interrupted, flat, asymmetric or have multiple peaks (45). Uroflowmetry can be useful by testing for these characteristics, but this may not be a tool that is available to most PCPs. Therefore, the PCP should be able to evaluate flow effectively simply by using terminology such as that mentioned above.

Treatment of OAB: behavioural and pharmacologic therapy

Behavioural therapy

The foundation for treating the patient with OAB is behavioural modification. The goal is to teach the patient the normal process of micturition and the mechanism by which symptoms define an abnormal physiology. Behavioural therapy should begin with patient education, but also can include bladder retraining and urge suppression techniques, dietary alterations, changing the timing of various concomitant medications (e.g. diuretics), and encouraging exercise and weight loss. Although most patients will require the addition of drug therapy, urinary incontinence literature shows that the combination of both behavioural and pharmacological therapies provides the greatest likelihood of positive outcome, compared with either intervention alone (46).

Pharmacologic therapy

The principle of pharmacologic management of OAB is to inhibit DO via antimuscarinic therapy. These agents exert their clinical effect through antagonistic action at cholinergic receptors on the detrusor muscle, preventing unwanted muscle contraction resulting from the parasympathetic acetylcholine release. As these agents are competitive antagonists, their effect is removed during the massive parasympathetic release of acetylcholine, which occurs with normal micturition, allowing for normal physiology (47). Antimuscarinics work via two potential roles: one on the motor pathway via central and peripheral actions that block a facilitory mechanism and stimulate an

inhibitory mechanism, and on the sensory pathway via central and peripheral actions that modulate afferent innervations.

Researchers and clinicians have provided significant contributions to the literature that support the diagnosis of male OAB, as well as showing therapy can be safe. A pivotal study by Abrams et al. (38) reported the results of utilisation of anticholinergic agents in selected male patients. In this study, men with elevated residuals (> 40% of maximum cystometric capacity) or prior genitourinary surgery (similar to our algorithm) were excluded and those remaining were offered antimuscarinic therapy. Urinary retention was reported only in one patient in the placebo group and the incidence of adverse events in those receiving medication was similar to those receiving placebo. Patients receiving anticholinergic therapy had significant improvement in bladder capacity, and increases in volume to first detrusor contraction and maximum cystometric capacity. The authors concluded that antimuscarinic therapy is safe and tolerable in men.

Five oral antimuscarinics have been approved for treatment: darifenacin, oxybutynin, solifenacin, tolterodine and trospium. Long-acting extended versions of these medications have better tolerability and titratable doses can be beneficial (48,49). The side effects of dry mouth and constipation are comparable with all the medications. There is currently a transdermal form of oxybutynin that limits the side effects of dry mouth and constipation, but has the adverse effect of skin irritation in certain patients. There are substantial data showing the safety of these drugs in male patients. All of them were reviewed for safety in men with BPH or BOO in a 2006 systematic review and meta-analysis by Blake-James et al. (50).

The patient and provider will generally be able to identify symptom relief within 2–4 weeks. On follow-up, it is prudent to check PVR to verify no retention of urine has occurred. If volume is ≤ 50 ml and the patient is satisfied, then continuation of medications with periodic follow-up is appropriate. The patient should be made aware that failure to void or a feeling of incomplete voiding is reason for urgent follow-up. If the symptoms are not resolved and the PVR is ≤ 50 ml, then the provider may want to increase the dose of medications, switch medications or refer. An evaluation of PVR > 50 ml is a reason to stop medication and seek a urologic consultation. However, some providers may wish to allow a slightly higher PVR, as the choice of 50 ml is somewhat arbitrary given that no specific value has been studied. For physicians who choose to utilise a more liberal PVR, we recommend close follow-up and more frequent evaluation of PVR.

Combination therapy

A brief note on combination therapy is prudent here, as the male patient frequently suffers from both OAB and BPH. As mentioned earlier, it is not uncommon for alpha blocker therapy to fail for reasons other than improper diagnosis. The patient's bothersome storage symptoms can be exacerbated by BPH (38). Although there is no formal guidance for the use of combination therapy, the conscientious provider may be able to elicit symptoms of both storage and voiding and treat appropriately as indicated. In a prospective study, 144 consecutive men with symptomatic and urodynamically confirmed BOO were subdivided into those with pure BOO (53%) and those with BOO plus DO (47%) (51). After the initial evaluation, all patients were treated with the alpha blocker doxazosin in escalating doses up to 4 mg/day for 3 months. Patients from both groups (with or without DO) who reported no improvement in symptoms were then assigned to combination therapy, which included immediate-release tolterodine 2 mg twice daily for an additional 2 months. Among men in the BOO + DO group, at the end of the initial 3-month treatment period with doxazosin alone, 65% reported no improvement and were then provided combination therapy. Of these patients assigned to combination therapy, 73% reported symptomatic improvement.

A 2005 open-label study evaluated the safety and efficacy of extended-release tolterodine in male patients with LUTS and in whom alpha blocker therapy had failed previously. After 6 months, the AUA-symptom score improved from 17.3 at baseline to 11.2 at 6 months. Of critical importance for the PCP is that no patients developed acute urinary retention (52).

Conclusions

There is conclusive evidence that many men are affected with LUTS. Here, we have reviewed data that show many of these men have OAB as the causative factor, rather than the traditionally thought BPH, although both are common. The majority of symptomatic men do not get treated (53). One can speculate on the many reasons for this lack of identification and treatment. Gaps in education, awareness and a lack of simplified screening tools may be at fault. Alternatively, providers may incorrectly assume that if LUTS were a problem, the patient would bring it up. Lastly, PCPs may fear that extensive evaluation will 'open a can of worms' with which they do not wish to deal.

This algorithm is proposed not as the 'end all' for the evaluation of LUTS in men, but as one mechanism to better facilitate proper evaluation of these patients. While many urologists might find it overly simple, it is intended only as a logical framework for evaluation and is intentionally kept simple to facilitate its use in the office of the busy PCP. Clearly, the PCP is the first line of contact for most of these patients. Men can be safely treated for LUTS in the PCP office, thereby saving the refractory cases for the specialist. If this were to occur, at least theoretically, more male patients with LUTS could be treated effectively and efficiently. This, in turn, could improve troublesome symptoms, and therefore quality of life, for those affected.

Acknowledgements

This study was sponsored by the Urologic Health Foundation (UHF), a non-profit organisation founded by clinicians, and was supported by an educational grant from Verathon Inc. Editorial support was provided by Educational Concepts in Medicine.

References

1 Hyman MJ, Groutz A, Blaivas JG. Detrusor instability in men: correlation of lower urinary tract symptoms with urodynamic findings. *J Urol* 2001; **166**: 550–3.
2 Van Venrooij GE, Van Melick HH, Eckhardt MD et al. Correlations of urodynamic changes with changes in symptoms and well-being after transurethral resection of the prostate. *J Urol* 2002; **168**: 605–9.
3 Kaplan SA, Ikeguchi EF, Santarosa RP et al. Etiology of voiding dysfunction in men less than 50 years of age. *Urology* 1996; **47**: 836–9.
4 Fawzy A, Fontenot C, Guthrie R et al. Practice patterns among primary care physicians in benign prostatic hyperplasia and prostate cancer. *Fam Med* 1997; **29**: 321–5.
5 Abrams P, Cardozo L, Fall M et al. The standardisation of terminology in lower urinary tract function: report from the standardisation sub-committee of the International Continence Society. *Urology* 2003; **61**: 37–49.
6 Dennis L, Griffiths K, Khoury S et al. Recommendations of the International Scientific Committee: the evaluation and treatment of lower urinary tract symptoms (LUTS) suggestive of benign prostatic obstruction. In: Denis L, Griffiths K, Khoury S, Cockett ATK, McConnell J, Chatelain C, Murphy C, Yoshida O. eds. *Proceedings of the Fourth International Consultation on Benign Prostatic Hyperplasia*. London: Health Publications, Ltd., 1998: 669–84.
7 Lee C, Cockett A, Cussenot K et al. Regulation of prostate growth. In: Chatelain C, Denis L, Foo KT, Khoury S, McConnell J. eds. *Proceedings of the Fifth International Consultation of Benign Prostatic Hyperplasia*, Chapter 3. London: Health Publications, Ltd., 2001: 79–106.
8 Abrams P, Cardozo L, Fall M et al. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. *Neurourol Urodyn* 2002; **187**: 167–78.
9 Ouslander JG. Management of overactive bladder. *N Engl J Med* 2004; **350**: 786–99.
10 Wein AJ. Pathophysiology and categorization of voiding dysfunction. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA, eds. *Campbell-Walsh Urology*, 9th edn. Philadelphia, PA: Saunders Elsevier, 2007: 1973–85.
11 Chapple CR, Artibani W, Cardozo LD et al. The role of urinary urgency and its measurement in the overactive bladder symptom syndrome: current concepts and future prospects. *BJU Int* 2005; **95**: 335–40.
12 Jaffe WI, Te AE. Overactive bladder in the male patient: epidemiology, etiology, evaluation, and treatment. *Curr Urol Rep* 2005; **6**: 410–8.
13 Stewart WF, Van Rooyen JB, Cundiff GW et al. Prevalence and burden of overactive bladder in the United States. *World J Urol* 2003; **20**: 327–36.
14 Berry SJ, Coffee DS, Walsh PC et al. The development of human benign prostatic hyperplasia with age. *J Urol* 1984; **132**: 474–9.
15 Wei JT, Calhoun E, Jacobsen SJ. Urologic diseases in America project: benign prostatic hyperplasia. *J Urol* 2005; **173**: 1256–61.
16 Rosenberg M. The sad, misunderstood prostate: understanding perceptions and reality. *Int J Clin Pract* 2006; **60**: 1148–9.
17 Jacobsen SJ, Girman CJ, Guess HA et al. New diagnostic and treatment guidelines for benign prostatic hyperplasia. Potential impact in the United States. *Arch Intern Med* 1995; **155**: 477–81.
18 O'Conor RM, Johannesson M, Hass SL et al. Urge incontinence. Quality of life and patients' valuation of symptom reduction. *Pharmacoeconomics* 1998; **14**: 531–9.
19 Bruskewitz RC. Quality of life and sexual function in patients with benign prostatic hyperplasia. *Rev Urol* 2003; **5**: 72–80.
20 Nickel JC. BPH: costs and treatment outcomes. *Am J Manag Care* 2006; **12** (Suppl. 5): S141–8.
21 McGhan WF. Cost effectiveness and quality of life considerations in the treatment of patients with overactive bladder. *Am J Manag Care* 2001; **7** (Suppl. 2): S62–75.
22 Haidinger G, Temml C, Schatzl G et al. Risk factors for lower urinary tract symptoms in elderly men. For the Prostate Study Group of the Austrian Society of Urology. *Eur Urol* 2000; **37**: 413–20.
23 Gades NM, Jacobson DJ, Girman CJ et al. Prevalence of conditions potentially associated with lower urinary tract symptoms in men. *BJU Int* 2005; **95**: 549–53.
24 Speakman MJ, Kirby RS, Joyce A et al. Guideline for the primary care management of male lower urinary tract symptoms. *BJU Int* 2004; **93**: 985–90.
25 van Kerrebroeck P, Abrams P, Chaikin D et al. for the Standardisation Sub-committee of the International Continence Society. The standardisation of terminology in nocturia: report from the Standardisation Sub-committee of the International Continence Society. *Neurourol Urodyn* 2002; **21**: 179–83.
26 Roehrborn CG, McConnell JD, Barry MJ. *Guidelines on the Management of Benign Prostatic Hyperplasia*. Linthicum, MD: American Urological Association, Education and Research, Inc., 2003.
27 Barry MJ, Fowler FJ Jr, O'Leary MP et al. and the Measurement Committee of the American Urological Association. The American Urological Association symptom index for benign prostatic hyperplasia. *J Urol* 1992; **148**: 1549–57.
28 Naslaund MJ, Costa FJ, Miner MM. Managing enlarged prostate in primary care. *Int J Clin Pract* 2006; **60**: 1609–15.
29 Suzuki S, Platz EA, Kawachi I et al. Intakes of energy and macronutrients and the risk of benign prostatic hyperplasia. *Am J Clin Nutr* 2002; **75**: 689–97.
30 Rohrmann S, Giovannucci E, Willett WC et al. Fruit and vegetable consumption, intake of micronutrients, and benign prostatic hyperplasia in US men. *Am J Clin Nutr* 2007; **85**: 523–9.
31 Miner M, Rosenberg MT, Perelman MA. Treatment of lower urinary tract symptoms in benign prostatic hyperplasia and its impact on sexual function. *Clin Ther* 2006; **28**: 13–25.

32 Lepor H, Williford WO, Barry MJ et al. for the Veterans Affairs Cooperative Studies Benign Prostatic Hyperplasia Study Group. The impact of medical therapy on bother due to symptoms, quality of life and global outcome, and factors predicting response. Veteran Affairs Cooperative Studies Benign Hyperplasia Study Group. *J Urol* 1998; **160**: 1358–67.
33 Lowe FC. Role of the newer alpha, -adrenergic receptor antagonists in the treatment of benign prostatic hyperplasia-related lower urinary tract symptoms. *Clin Ther* 2004; **26**: 1701–13.
34 Kirby RS. Doxazosin in benign prostatic hyperplasia. Effects on blood pressure and urinary flow in normotensive and hypertensive men. *Urology* 1995; **46**: 182–6.
35 Kirby RS. Terazosin in benign prostatic hyperplasia. Effects on blood pressure in normotensive and hypertensive men. *Br J Urol* 1998; **82**: 373–9.
36 Kaplan SA. Update on the American Urological Association guidelines for the treatment of benign prostatic hyperplasia. *Rev Urol* 2006; **8** (Suppl. 4): S10–7.
37 McConnell JD, Roehrborn CG, Bautista OM et al. for the Medical Therapy of Prostatic Symptoms (MTOPS) Research Group. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. *N Engl J Med* 2003; **349**: 2387–98.
38 Abrams P, Kaplan S, De Koning Gans HJ et al. Safety and tolerability of tolterodine for the treatment of overactive bladder in men with bladder outlet obstruction. *J Urol* 2006; **175**: 999–1004.
39 McNeill SA, Hargreave TB, Geffriaud-Ricouard C et al. Postvoid residual urine in patients with lower urinary tract symptoms suggestive of benign prostatic hyperplasia: pooled analysis of eleven controlled studies alfuzosin. *Urology* 2001; **57**: 459–65.
40 Kolman C, Girman CJ, Jacobsen SJ et al. Distribution of post-void residual urine in randomly selected men. *J Urol* 1999; **161**: 122–7.
41 Goode PS, Locher JL, Bryant RL et al. Measurement of postvoid residual urine with portable transabdominal bladder ultrasound scanner and urethral catheterization. *Int Urogynecol J Pelvic Floor Dysfunct* 2000; **11**: 296–300.
42 Coombes GM, Millard RJ. The accuracy of portable ultrasound scanning in the measurement of residual urine volume. *J Urol* 1994; **152** (6 part 1): 2083–5.
43 Byun SS, Kim HH, Lee E et al. Accuracy of bladder volume determinations by ultrasonography: are they accurate over entire bladder volume range? *Urology* 2003; **62**: 656–60.
44 Ockrim JL, Laniado ME, Patel A et al. A probability based system for combining simple office parameters as a predictor of bladder outflow obstruction. *J Urol* 2001; **166**: 2221–5.
45 Abrams P. *Urodynamics*, 3rd edn. London, England: Springer, 2005.
46 Burgio KL, Locher JL, Goode PS. Combined behavioral and drug therapy for urge incontinence in older women. *J Am Geriatric Soc* 2000; **48**: 370–4.
47 Andersson K-E. Antimuscarinics for treatment of overactive bladder. *Lancet Neurol* 2004; **3**: 46–53.
48 Steers W, Corcos J, Foote J et al. An investigation of dose titration with darifenacin, an M_3-selective receptor antagonist. *BJU Int* 2005; **95**: 580–6.
49 Chapple CR, Martinez-Garcia R, Selvaggi L et al. for the STAR study group. A comparison of the efficacy and tolerability of solifenacin succinate and extended release tolterodine at treating overactive bladder syndrome: results of the STAR trial. *Eur Urol* 2005; **48**: 464–70.
50 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* 2006; **99**: 85–96.
51 Lee JY, Kim HW, Lee SJ et al. Comparison of doxazosin with or without tolterodine in men with symptomatic bladder outlet obstruction and overactive bladder. *BJU Int* 2004; **94**: 817–20.
52 Kaplan SA, Walmsley K, Te AE. Tolterodine extended release attenuates lower urinary tract symptoms in men with benign prostatic hyperplasia. *J Urol* 2005; **174**: 2273–6.
53 Kaplan S, Naslund M. Public, patient, and professional attitudes towards the diagnosis and treatment of enlarged prostate: a landmark national US survey. *Int J Clin Pract* 2006; **60**: 1157–65.

Paper received April 2007, accepted May 2007

