The evaluation of benign prostatic hyperplasia (BPH) has evolved dramatically during the past 25 years. If an adult male went to see a urologist in the late 1980s with lower urinary tract symptoms (LUTS) he may have been offered a non-selective alpha-blocker but more than likely a transurethral resection of the prostate (TURP).
If he returned a year later with any persistent or recurrent symptoms, another TURP would have been scheduled. Our working knowledge of the lower urinary tract was far from complete and the role of the bladder was infrequently contemplated. Fortunately this has changed for the better. The physiology of the bladder and the neural control is now well documented and better understood. The bladder is now known to be a significant contributor to LUTS as it relates to the classic overactive bladder (OAB) symptoms. Whether OAB occurs as a result of obstruction or as a concomitant process in an aging bladder is still open for debate. A thorough evaluation of male LUTS is incomplete without also evaluating the bladder, such that medications for OAB are part of the algorithm for male LUTS.

Today, treatment of male LUTS includes a variety of medications to treat BPH as well as office-based minimally invasive techniques. Although TURP remains the surgical gold standard, there are newer techniques with bipolar technology, laser ablation and enucleation. The following discussion of LUTS in general and treatment for BPH should help the practicing clinician understand the work-up and treatment options offered to patients.

**Male LUTS**

Male LUTS is a non-specific term commonly used to describe storage and/or voiding disturbances of the micturition cycle. Most often these symptoms are attributed to BPH or bladder outlet obstruction (BOO) from an enlarged prostate. Although there is a high prevalence of BPH in elderly men, up to 40% in men in their fifth decade and 90% in men in their ninth decade, most recent published literature has also identified the bladder as a contributor to irritative voiding symptoms, leading to new evidence that the prostate is not always the problem. Interestingly, more recent reports demonstrate only a weak correlation between prostate size, severity of BOO, and severity of symptoms and suggest that not all men with large prostates have bothersome LUTS while others with minimal enlargement may demonstrate significant symptoms. A strong correlation, however, does exist between serum prostate-specific antigen (PSA) levels and prostate volume, with higher PSA levels often detected in patients with significant prostatic enlargement leading to the concept of age-specific PSA ranges as described by Oesterling et al in 1993. LUTS may be due to structural or functional abnormalities of any part of the lower urinary tract, which includes the bladder, bladder neck, prostate, distal sphincter mechanism and urethra. The lower urinary tract is directly under neuronal control (both sympathetic and parasympathetic) and therefore abnormalities of the peripheral and/or central nervous systems (CNS) can also lead to disturbances in micturition.

In addressing male LUTS it is essential to establish a common set of definitions and nomenclature and also to review the normal micturition cycle.

**Nomenclature**

Some of the names and terms used in the BPH-LUTS field of study include the following:

- **Prostatic enlargement** is the
term applied to a clinically enlarged prostate, ie, diagnosed via digital rectal examination (DRE) or imaging such as CT scan, MRI or transrectal ultrasound (TRUS), without histological evidence. DRE provides a relatively crude assessment of size and is subject to provider interpretation. One of the major drawbacks of the DRE is the lack of palpation of the median lobe; therefore patients may demonstrate obstructive symptoms despite a “normal” DRE. In 1999, Rhodes et al determined that prostate volume increased with age across all age groups and the average annual change in prostate volume is approximately 1.6%.  

More objective data on size can be obtained via imaging modalities mentioned above. Gland sizes are often labeled in grams or grades. A 30-g prostate is considered “normal size”—roughly equivalent to the size of a walnut. There is no consensus regarding extent of volumetric enlargement to establish the diagnosis of an enlarged prostate; however, prostate volume of approximately 20 mL or less is generally regarded as normal.

**Benign prostatic hyperplasia**  
Most men with voiding complaints are often labeled with “BPH”. In itself, BPH is strictly a histological diagnosis, meaning that a patient must undergo biopsy or TURP to obtain tissue for pathological examination. BPH is hyperplasia (not “hypertrophy” as it is often reported) and proliferation of the stromal and epithelial elements of the prostate that most commonly occurs in the transition zone of the prostate and the periurethral glands. This results in volumetric enlargement of the prostatic gland, which can encroach the bladder neck and prostatic urethra, leading to obstructive voiding symptoms, or BOO.

Subclassification of BPH into microscopic, macroscopic, and clinical BPH has been proposed, where microscopic BPH refers to histological diagnosis, macroscopic to diagnosis based on physical examination including DRE and imaging, and clinical BPH referring to symptomatology of LUTS, including incomplete emptying and urinary retention.

**Bladder outlet obstruction** is the generic term for all forms of obstruction to the bladder outlet such as an enlarged prostate, urethral stricture, bladder stones causing ball-valving during voiding, bladder neck contracture, detrusor-sphincter dyssynergia, and, less likely, meatal stenosis.

**Benign prostatic obstruction** is specific for obstruction of urine flow secondary to an obstructing prostate and is objectively proven by pressure flow studies or deduced from urodynamic studies.

**Micturition cycle**  
The lower urinary tract comprises the bladder, the bladder neck, prostate, urethra, urethral meatus and 2 urethral sphincters, the internal (smooth muscle) sphincter at the bladder neck and proximal urethra and the external (striated muscle) sphincter of the membranous urethra. These structures are interrelated and together function in maintaining the micturition cycle—a series of coordinated events that ensures bladder filling, urine storage without leakage and periodic volitional expulsion of urine to completion, all at low pressure. Any dysfunction of the lower urinary tract members can lead to a disruption of normal voiding.

Perhaps the best and most succinct description of the micturition cycle has been proposed by Alan Wein, MD. In Wein’s model, the cycle is divided into 2 separate and discrete phases:
1. Bladder filling/urine storage
2. Bladder emptying/voiding

These phases are under neuronal control and require inhibition of the voiding reflex during the storage phase and activation of the voiding reflex with inhibition of storage reflexes during the emptying phase. Bladder filling and urine storage require passive filling of the bladder with increasing volume under low pressure. This is referred to as bladder compliance. This is under sympathetic control via the hypogastric nerve which relaxes the detrusor muscle while simultaneously contracting the internal sphincter located at the bladder neck.

The external striated sphincter under the influence of the peripheral pudendal nerve is concurrently contracted. A closed bladder outlet is required to

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**Table 1. Innervations of the lower urinary tract**

<table>
<thead>
<tr>
<th>Type</th>
<th>Origin</th>
<th>Effect on detrusor muscle</th>
<th>Effect on sphincteric muscles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypogastric</td>
<td>Sympathetic</td>
<td>Relaxes</td>
<td>Contracts</td>
</tr>
<tr>
<td>Pelvic</td>
<td>Parasympathetic</td>
<td>Contracts</td>
<td>Relaxes</td>
</tr>
<tr>
<td>Pudendal</td>
<td>Somatic (peripheral)</td>
<td>Does not affect detrusor</td>
<td>Contracts</td>
</tr>
</tbody>
</table>

prevent leakage of urine as is absence of involuntary bladder contractions (detrusor overactivity [DO]). An intact sensory reflex arc is activated once the bladder has reached capacity and triggers the sensation to void.

Bladder emptying and voiding is triggered by a full bladder. It involves coordinated contractions of bladder smooth muscles, increasing bladder pressure that is less than 40 cm H₂O to prevent upper tract damage, relaxation of the smooth and striated sphincters and subsequent active expulsion of urine without anatomic obstruction. This process is under the control of the parasympathetic pelvic nerves which trigger coordinated detrusor contractions with simultaneous relaxation of the sphincteric muscles.6

The symptoms of the various dysfunctions in voiding are then based upon these 2 phases.

Dysfunctions in the micturition cycle: filling/storage failure
Storage symptoms occur during the filling and storage phase of micturition. Some of the most common symptoms are:

- **Urgency** – A sudden compelling desire to void that is difficult to defer.
- **Daytime frequency** – A patient’s perception that he voids too often by day. Healthy adults generally void every 3 to 4 hours with a normal fluid intake (approximately 64 ounces of fluid daily).7
- **Nocturia** – The need to wake at night 1 or more times to void. It is important to differentiate nocturia from excessive nighttime urine production or nocturnal polyuria and sleep disorders, including sleep apnea.
- **Urgency incontinence** – Involuntary leakage of urine, accompanied by, or immediately preceded by urgency.

Failure of the bladder to fill adequately and/or store urine can be due to several reasons outlined below:

- **Decreased compliance** may be secondary to neurologic injury or disease or may be the result of any process that impairs the viscoelastic or elastic properties of the bladder wall. It is primarily due to an increase in the collagen component of the bladder wall making it less elastic and more fibrotic. Etiologies include diseases that cause hypertrophy of the bladder detrusor muscle such as chronic inflammation, BOO and bladder hypertonicity from neurological disease. Loss of compliance by replacement of normal stromal tissue by type III collagen is permanent and generally unresponsive to treatments such as pharmacologic manipulation, hydro distention or nerve resection. Ultimately this results in a low-capacity bladder leading to frequent urination of small volumes.

- **Bladder overactivity** is another reason for failure of the bladder to fill adequately and/or store urine. There are several commonly used terms in literature with overlapping definitions for symptoms relating to bladder overactivity; hence it is important to clarify these terms as they relate to bladder pathophysiology.

  - **Overactive bladder** is a symptom-based condition and defined by the International Continence Society (ICS) standardization committee as urgency, with or without urgency incontinence, referred to as OAB wet or OAB dry, respectively. Overactive bladder is usually also associated with frequency and nocturia. It is important to note that urgency is the key component here and urgency with at least 1 other symptom is essential to diagnose OAB.8 Furthermore, infection and other obvious pathologies must be excluded prior to making a diagnosis of OAB. It affects approximately 12% of adult males and females8 and is synonymous with urgency and urgency/frequency syndrome. These symptoms often coexist with classic obstructive symptoms and often do not resolve with the
treatment of the bladder outlet alone. This has led to the relatively new treatment paradigm of combination therapy consisting of alpha-blockers plus anticholinergics or beta-3 agonists to treat BOO with concurrent OAB symptoms.

- **Detrusor hyperreflexia** is specific for involuntary bladder contractions most often noted in patients with a neurologic cause. The primary causes for this entity are neurologic diseases, specifically suprapontine disorders such as cerebrovascular accidents, dementia, cerebral palsy, head injury, multiple sclerosis (MS) and brain tumors. These disorders diminish cortical inhibition as is seen in other upper motor neuron lesions, resulting in overactivity of the lower motor neuronal component and reduced control of the micturition reflex. Detrusor hyperreflexia is synonymous with neurogenic DO.

- **Unstable bladder** is an ICS-designated term for bladder overactivity where there is no obvious cause for detrusor contractions. It is synonymous with idiopathic DO.

- **Detrusor overactivity** is a urodynamic observation. It is characterized by involuntary detrusor contractions noted during the filling phase of the study. These may be spontaneous or provoked. It is synonymous with detrusor instability.

Overall, bladder overactivity results in frequent urination, often before the bladder has reached full capacity.

- **Sphincter dysfunction**
  Decreased outlet resistance from neurologic or iatrogenic causes results in an open bladder neck and/or loss of voluntary control during the filling phase resulting in either constant leakage of urine or leakage at low volumes. Neurologic etiologies include sacral lesions such as spina bifida, MS, diabetes mellitus and myelomeningocele. These disrupt innervation of structural elements of the smooth or striated sphincter, or both. Iatrogenic causes are usually from surgical injury during a TURP or prostatectomy. Incontinence after TURP typically occurs because of mechanical trauma of the external striated sphincter at the level of the verumontanum. Prostatectomy can cause both nerve damage as well as mechanical trauma.

**Dysfunctions in the micturition cycle: emptying/voiding failure**
Voiding symptoms occur at the time of urine flow. Some of the most common symptoms are:
- **Slow stream** – the individual’s perception of reduced urine flow with or without splitting or spraying of the urine stream.
- **Intermittency** – urinary flow that starts and stops intermittently on 1 or more occasions during micturition.
- **Hesitancy** – difficulty in initiating flow of urine. Results in a delay in micturition.
- **Straining to void** – abdominal muscular effort is utilized to initiate urinary flow. It may also be used to maintain flow and ensure complete bladder emptying.
- **Terminal dribble** – trickling or dribbling for urinary flow at the end of micturition.
- **Dysuria** – discomfort, burning or painful sensation during micturition.

Failure to empty can occur for a variety of reasons:
- **Bladder underactivity** – Failure of bladder contractility or underactivity

### Table 2. Male lower urinary tract symptoms

<table>
<thead>
<tr>
<th>Obstructive (BPH)</th>
<th>Irritative (OAB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hesitancy</td>
<td>Urgency</td>
</tr>
<tr>
<td>Poor flow/weak stream</td>
<td>Frequency</td>
</tr>
<tr>
<td>Intermittency</td>
<td>Nocturia</td>
</tr>
<tr>
<td>Straining to void</td>
<td>Urge incontinence</td>
</tr>
<tr>
<td>Terminal dribble</td>
<td>Stress incontinence</td>
</tr>
<tr>
<td>Prolonged urination</td>
<td>Mixed incontinence</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>Overflow incontinence</td>
</tr>
</tbody>
</table>

may result in significant residual urine (elevated post void residual/incomplete emptying) or complete inability to initiate micturition (urinary retention). This may be temporary or permanent and etiologies include failure or impairment in one of the neuromuscular mechanisms necessary for initiating and maintaining normal detrusor contractions.

**Non-neurogenic causes of bladder underactivity include the following:**

- Bladder overdistention resulting in reversible myogenic stretch injury of the muscle fibers, e.g., acute urinary retention. Treatment typically consists of bladder rest with a temporary indwelling Foley catheter. Chronic myogenic stretch/distention may lead to myogenic failure over time, resulting in irreversible damage.
- Medications such as anticholinergics, antidepressants and opioids can cause temporary inhibition of detrusor contractions. Effects are generally reversible with titration or discontinuation of the offending agent.
- Urinary tract infections are irritable to bladder urothelium, resulting in decreased contractions of the detrusor muscle.
- Constipation, ileus, small bowel obstruction: cause a reflex mechanism that temporally inhibits the pontine micturition center. Resolution of bowel pathology results in resolution of bladder inactivity.

**Neurogenic causes of bladder underactivity include the following:**

- CNS etiologies – demyelinating disorders such as MS or degeneration of the basal ganglia as seen in Parkinson disease have subsequent effects on the efferent pathways to the bladder, resulting in acontractility.
- Iatrogenic causes such as aggressive pelvic surgery can damage surrounding nerves. The pelvic surgeries most commonly associated with voiding dysfunction include abdominoperineal resection and radical hysterectomy that may result in damage to the pudendal or parasympathetic nerves, respectively.\(^{10}\)
- Striated sphincter dyssynergia occurs in patients with neurological injury. It is a discoordination between bladder contraction and outlet relaxation as is seen in the normal micturition cycle. Also commonly referred to as detrusor external sphincter dyssynergia, it is the simultaneous activation of the external sphincter during detrusor contractility, causing an obstruction of urinary flow.
Outlet dysfunction – When it comes to bladder failure, outlet dysfunction must also be considered (see striated sphincter dysnergia on page 8).

Some common causes of anatomic outlet obstruction include the following:
- Prostatic enlargement.
- Bladder neck contracture typically secondary to previous surgery such as TURP, prostatectomy, cystoscopies or trauma from Foley catheter placements.
- Urethral strictures can be caused by urethral trauma from prior surgeries such as TURP, prostatectomy, Foley catheterizations, or from prior sexually transmitted diseases. Strictures can present as slow stream with difficulty emptying the bladder. Urinary stream can be weak, splitting with resultant spraying during micturition.

Evaluating and examining patients
Initial evaluation should comprise a detailed history and physical examination.

History
History should include the onset, duration, and severity of lower urinary tract symptoms. General health issues along with medications should be reviewed, as several common medications to treat ailments such as depression, chronic obstructive pulmonary disease, asthma and allergies have been associated with LUTS.

Other components of the history should include sexual function history and review of any previous surgical procedures, particularly those pertaining to the genitourinary tract. If there is a history of urinary incontinence, then patients should be questioned regarding any previous neurologic symptoms, injury or disease.

Furthermore, the patient’s overall performance status should also be evaluated for possible surgical interventions.

Physical examination
A focused physical examination should be performed. Attention should be directed to the suprapubic region for assessment of palpable bladder distention. A neurological examination should be performed to assess overall motor and sensory function. Particular attention should be paid to the perineum and lower limbs.

Digital rectal examinations should be performed to evaluate anal sphincter tone and the prostate gland. The prostate should be evaluated for consistency, shape and abnormalities suggestive of prostate cancer such as nodules. As previously mentioned, DREs are a crude measure of prostatic size. Furthermore DREs only allow evaluation of lateral lobe hypertrophy and abnormalities. The lateral lobes correlate with the peripheral zone which is most commonly associated with prostate cancer. Therefore patients with predominant median lobe hypertrophy may have a palpably normal prostate of appropriate size on DRE.

Laboratory data/imaging
As part of the evaluation process, the following laboratory data and imaging testing should be considered:

- Urinalysis by dipstick testing or microscopic examination of sediment should be undertaken to rule out urinary tract infection, hematuria, proteinuria or other pathological findings (eg, glucosuria, ketonuria etc).
- PSA testing must be performed for an abnormal DRE. In the setting of a normal physical examination, however, PSA testing is recommended in patients with a life expectancy greater than 10 years and/or for patients in whom a diagnosis of prostate cancer would modify the management approach. Furthermore, the risks and benefits of PSA testing should be discussed with the patient as well as the possibility of subsequent transrectal ultrasound guided biopsy.
- Serum creatinine should be assessed for evaluation of renal function.

Objective assessment and diagnostic testing

Symptom Assessment
To assess overall bother from

![Figure 2. Effects of prostatic hypertrophy.](image-url)
symptoms, there are several well-designed and validated quantitative assessment tools that have been developed. One of which is the International Prostate Symptom Score (IPSS). This is a reproducible, validated index designed to determine disease severity and response to therapy and also to assess overall quality of life. The questionnaires may be filled in by the patient at home before the appointment or at the time of office visit.

**Frequency Volume Chart**

Frequency Volume Chart (voiding diary) is another assessment tool. This voiding diary is a record that details the patient’s voiding episodes. It is designed to evaluate the number of voids and volume at each void for several 24-hour periods (usually 3). It is also useful in identifying patients with nocturnal polyuria or excessive fluid intake. It is most useful when nocturia is the predominant symptom.

**Uroflowmetry**

Uroflowmetry is a simple noninvasive urodynamic measurement in which a patient urinates into a device that measures the volume/time of urine accumulation. The amount of voided volume, voiding time, average flow rate, and maximum flow rate are measured. This test is useful in identifying patients with obstructive voiding symptoms and in monitoring the response to therapy.

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**Figure 3.** Basic management of LUTS in men in primary care.


rate, and maximum flow rate (Qmax) are measured. A Qmax >15mL/s is considered normal while <10mL/s is suggestive of outlet obstruction.

**Post void residual (PVR)**

Per American Urological Association guidelines, evaluation of PVR is optional. It can be useful as part of the initial evaluation. Once therapy has been initiated, subsequent PVRs may be helpful in assessing improved bladder emptying and success of therapy. PVRs are determined by noninvasive transabdominal ultrasonography.

Of note, PVR does not correlate with the severity of LUTS, the presence of BOO, or treatment outcomes. An elevated PVR can be found with obstruction along with detrusor decompensation and bladder dysfunction.

PVR is strongly recommended prior to initiating anticholinergic therapy for OAB symptoms to rule out incomplete bladder emptying. Use of these medications in patients with incomplete emptying (due to detrusor underactivity or BOO) may pivot the patient over into acute urinary retention.

**Pressure flow and urodynamic studies (UDS)**

UDS is an additional optional study and is considered the gold standard for diagnosis of overactive bladder secondary to uninhibited detrusor contractions.

UDS involves simultaneous multi-channel measurements of bladder and abdominal pressures during the filling/storage phase and urinary flow rates during the voiding phase of micturition. The hallmark pattern of BOO is high detrusor pressure with a low urinary flow rate. UDS can then be used to distinguish BOO vs detrusor underactivity by relating detrusor pressure at maximum urinary flow rate to the maximum flow rate.

Indications for UDS include the following: pre-operative evaluation of bladder function prior to invasive procedure; men who have previously failed medical therapy for LUTS; and male patients with neurological disease.

The severity of LUTS is the strongest independent risk factor for ED.

**LUTS and erectile dysfunction**

An association between LUTS caused by BPH and erectile dysfunction (ED) has been established, although the exact mechanism is still unclear. What is known is that both LUTS and ED predominately occur in the aging male. Furthermore, the Multinational Survey of the Aging Male study established that the severity of LUTS is the strongest independent risk factor for ED.

Several mechanisms have been proposed and are being further investigated, including autonomic hyperactivity (increased sympathetic tone), vascular disease, role of nitric oxide (NO), pelvic ischemia secondary to atherosclerosis and age-related hormonal alterations.

Most recently, tadalafil (Cialis), a commonly used phosphodiesterase type 5 inhibitor (PDE5I) for ED, received US Food and Drug Administration (FDA) approval for use in patients with BPH. Several studies showed an improvement in IPSS scores and BPH-related urinary symptoms in men using 5 mg daily dosing of Cialis for concurrent ED.

**Referral to urology**

If the primary care physician is comfortable with the basic initial evaluation and diagnosis of bothersome LUTS due to an enlarged prostate, then it is not unreasonable to initiate a trial of medical therapy. Urological referral and evaluation is recommended in the following instances:

- Persistent symptoms after initial medical treatment
- LUTS with OAB symptoms
- Men with incontinence
- Men <45 years of age
- Abnormal prostate on examination
- Presence of microscopic or gross hematuria
- Men who desire surgical treatment

**Individualized treatment**

Given the multitude of factors described above that may contribute to male LUTS, treatment is individualized to address the inciting factor(s). If the baseline symptoms are not bothersome to the patient, then a trial of watchful waiting may be pursued.

For patients with mildly bothersome symptoms, initial treatment with behavioral and lifestyle modification with or without biofeedback may alleviate symptoms. Lifestyle changes include avoiding or decreasing fluid intake prior to bedtime to decrease episodes of nocturia. Reduction in consumption of mild diuretics such as caffeine and alcohol may also be helpful as well as attenuating timing of diuretic medications so that they are taken during daytime waking hours instead of bedtime. Training in biofeedback promotes pelvic relaxation allowing improvement in bladder emptying and thus urgency symptoms and urinary frequency.

If storage symptoms predominate without evidence of BOO, then consideration must be given to...
overactive bladder due to idiopathic DO. A combination of behavioral modification along with biofeedback and anticholinergic medication has proven successful. Prior to starting anticholinergic therapy, it is prudent to ensure adequate baseline bladder emptying to risk tipping the patient into complete urinary retention.

**Medical therapy**

Initial treatment for BOO secondary to BPH is generally pharmacologic, consisting of alpha-blockers, 5-alpha reductase inhibitors, PDE5Is, or a combination of these agents. This is the recommended option for patients with mild-to-moderate symptoms with no clear indication for surgical intervention.

The ideal candidates for medical therapy are men with bothersome LUTS that negatively impacts quality of life. The patients must be counseled on lifetime commitment to medical therapy, provided the drug is effective with minimal or tolerable adverse side effects. Discussion should also include possible surgical intervention in the event that there is progression of the patient’s symptoms or if symptoms persist despite an adequate trial of medical therapy.

Patients initiated on medical therapy should be followed at appropriate intervals with periodic assessment to evaluate treatment success or failure, possible adverse side effects and to determine if alterations in the treatment plan are indicated. Once patients are stable on an appropriate medical regimen, annual follow-up is recommended.

**Alpha-1 blockers (A1B)**

There are 5 approved A1Bs in the United States: terazosin (Hytrin), doxazosin (Cardura), tamsulosin (Flomax), alfuzosin (Uroxatral), and silodosin (Rapaflo). These agents block alpha-1 adrenergic receptors causing relaxation of prostatic and bladder neck smooth muscle. Doxazosin, terazosin and alfuzosin are all non-selective A1Bs while tamsulosin and silodosin are considered selective A1Bs.

Partial benefit with improvement in symptoms can be seen in as little as 1 week, while full therapeutic effect is achieved in 6 to 8 weeks. Dizziness, asthenia, orthostatic hypotension and retrograde ejaculation are the most common side effects encountered with A1Bs.

Orthostatic hypotension is more common with nonselective A1Bs because of the presence of alpha-1 receptors in the smooth muscle of the systemic vasculature. Therefore dose titration is recommended when initiating therapy with these agents. Terazosin is initiated at 1 mg daily at bedtime and titrated to 5 or 10 mg/d over a period of 1 to 2 weeks until appropriate symptom relief is noted. Doxazosin is usually initiated at 1mg daily at bedtime and titrated to a maximum dose of 8 mg/d over a period of 1 to 2 weeks. Tamsulosin and silodosin each have a set dose of 0.4 mg and 8 mg once daily, respectively. Dosing at bedtime is generally recommended to decrease hypotensive episodes and syncope with resultant falls in the elderly population. Selective alpha-blockers have a higher incidence of ejaculatory disorders, specifically retrograde ejaculation.

Intraoperative floppy iris syndrome (IFIS) is a well-recognized complication of cataract surgery that has been associated with tamsulosin's cross reactivity with the alpha 1A receptor subtype in the iris dilator muscle. Clinical manifestations include poor preoperative pupil dilation, iris billowing and prolapse, and progressive intraoperative miosis. IFIS can also occur up to several years after discontinuation of tamsulosin.

In a patient with a known diagnosis of cataract, prescribing physicians may wish to consider involving the patient's cataract surgeon before initiating therapy with tamsulosin or alpha-adrenergic blocker treatment. Patients should be encouraged to report any prior or current history of alpha 1 antagonist use to patients initiating therapy with tamsulosin or silodosin.

**Table 3. Medication for BPH/LUTS**

<table>
<thead>
<tr>
<th>Category</th>
<th>Brand Name</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha-blockers – non uroselective</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Terazosin</td>
<td>Hytrin</td>
<td>BPH</td>
</tr>
<tr>
<td>Doxazosin</td>
<td>Cardura</td>
<td>BPH</td>
</tr>
<tr>
<td>Alpha-blockers – uroselective</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alfuzosin</td>
<td>Uroxatral</td>
<td>BPH</td>
</tr>
<tr>
<td>Silodosin</td>
<td>Rapaflo</td>
<td>BPH</td>
</tr>
<tr>
<td>Tamsulosin</td>
<td>Flomax</td>
<td>BPH</td>
</tr>
<tr>
<td>Phosphodiesterase-5 inhibitors</td>
<td>Cialis</td>
<td>BPH and ED</td>
</tr>
<tr>
<td>5-alpha reductase inhibitors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dutasteride</td>
<td>Avodart</td>
<td>BPH</td>
</tr>
<tr>
<td>Finasteride</td>
<td>Proscar</td>
<td>BPH</td>
</tr>
</tbody>
</table>
their ophthalmic surgeon before undergoing any eye surgery.

- **5-alpha reductase inhibitors (5ARIs)**

5-alpha reductase inhibitors inhibit the conversion of testosterone to its more potent metabolite, dihydrotestosterone (DHT). The main effect of 5ARIs is to reduce the static, obstructive component of BPH by reducing prostate size. Reduction of DHT results in epithelial atrophy and up to a maximum of 25% reduction of prostate volume that is achieved, on average, within 6 months of initiating therapy. This also subsequently reduces the average total serum PSA value by approximately 50%. PSA surveillance while taking 5ARIs has been the subject of several published studies. A true PSA value of a patient on 5ARI is roughly calculated by multiplying the serum PSA by 2.

Two 5ARIs are currently available: finasteride (Proscar) and dutasteride (Avodart). Finasteride is a type II 5-alpha reductase inhibitor with a dosing regimen of 5 mg per day, and dutasteride is a dual inhibitor of both type I and type II 5-alpha reductase with a daily dosing of 0.5 mg. Long-term placebo-controlled studies of both agents show significant improvements in IPSS and Qmax after a minimum of 3 months of therapy. Both also decrease the risk of acute urinary retention and delay need for surgery. Significant adverse events include ejaculatory disorder, erectile dysfunction, decreased libido, and gynecomastia. Hypotension is less of a concern with these agents as they have no effect on alpha receptors.

- **Phosphodiesterase type 5 inhibitors**

The PDE5Is class is a relatively new addition to the treatment armamentarium for BPH-LUTS. Vardenafil (Staxyn, Levitra), sildenafil (Viagra), and tadalafil (Cialis) have all been studied for their effects in reducing LUTS; however, in the United States, only tadalafil is approved for this indication.

The exact mechanism of action of PDE5Is is unknown, but it is believed that they increase signaling of the NO/cGMP pathway which reduces smooth muscle tone in the lower urinary tract. Similar to alpha-blockers, PDE5Is have no impact on prostate growth.

Treatment with a PDE5i is appropriate for the symptomatic patient who has identified obstruction, bother, and a PSA of <1.5 ng/mL. Since PDE5Is improve ED, a patient with both BPH and any degree of ED, could benefit from a medication that can treat both conditions.

Common side effects of these agents include headache, back pain, dizziness and dyspepsia. 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-artertial anterior ischemic optic neuropathy. Cardiac status must be assessed for patient risk before taking these medications.

- **Combination therapy**

Combination therapy with both alpha-blocker and 5-alpha reductase inhibitor drugs has been evaluated in multiple studies. All studies have shown that combination therapy is superior to monotherapy for reduction in IPSS scores and episodes of urinary retention along with improvement in Qmax and delaying clinical progression of BPH and the need for surgical intervention.

To date, Jylha (dutasteride and tamsulosin) is the only FDA-approved combination therapy administered via a single pill. However, it can be cost prohibitive and therefore alternate and equally effective therapy can be administered via 2 separate pills.

The other combination therapy is for men with symptoms of both BPH and OAB. Recent data suggest that the use of alpha-blockers and anticholinergics or beta-3 agonists is acceptable in individuals with combination symptoms. These patients require closer follow-up with uroflow and PVR as they are at increased risk for elevated residual urine.

- **Herbal therapy**

Phytotherapy for BPH is marketed in many health stores. The most common agents advertised are saw palmetto (Serenoa repens), African plum (Pygeum africanum), South African Star Grass (Hypoxis rooperi) and Beta-sitosterol.

While saw palmetto remains the most commonly used phytotherapy agent, the mechanism of action is unknown. Furthermore, well-designed placebo controlled trials have failed to show any clinical, objective or subjective improvement in patient symptoms. To date, neither the FDA, the American Urological Association, the European Association of Urology, or the International Consultation on Urological Diseases recommend or endorse these products for the treatment of male LUTS.

- **Surgical treatment**

There are several indications for surgical intervention of men diagnosed with enlarged prostates. Individuals presenting with recurrent urinary
Tract infections, persistent or recurrent urinary retention with or without renal insufficiency, progression of BPH-related symptoms despite maximal medical therapy, bladder calculi and recurrent gross hematuria may develop life threatening consequences if the bladder outlet obstruction remains unaddressed. Therefore, surgical intervention and urological evaluation is warranted.

- Minimally invasive
Intraprostatic stents are an alternative are an alternative to an indwelling catheter for patients who are unfit for surgery.

UroLume® is an endourethral prostatectomy manufactured by American Medical Systems (Minnetonka, Minnesota). It is a woven tubular mesh that maintains its position in the urethra by outward external pressure, thus maintaining the patency of the prostatic urethra. Reports of irritative voiding symptoms, painful ejaculation and stent migration have contributed towards the decreased use of this product.

The UroLift System by NeoTract (Pleasanton, California) is a new nonablative in-office procedure. This technique utilizes the placement of intraprostatic non-absorbable sutures into the lateral lobes of the prostate, essentially pulling apart the lobes and increasing the size of the urethral lumen and creating an open channel.

Recently published 2-year data showed improvement in IPSS scores by 42% and peak flow rates by at least 30%, in patients undergoing this treatment.

Minimal side effects have been noted with no reported episodes of anejaculation or retrograde ejaculation.

- Ablation/Photovaporization
Transurethral needle ablation of prostate (TUNA) uses low-level radiofrequency energy delivered to the prostate with needles. The heat generated increases the intraprostatic temperature, resulting in necrosis of the hyperplastic tissue.

TUNA is best shown to improve IPSS scores and obstructive symptoms in patients with prostate glands less than or equal to 60 g and with predominantly lateral lobe hypertrophy.

Laser ablative and enucleation procedures are gaining more momentum in the treatment of BPH. These modalities emit light at different wavelengths (based on the type of laser utilized) that are preferentially absorbed by prostatic tissue than surrounding water. Absorption leads to coagulation, necrosis and sloughing off of the hyperplastic tissue.

Recent advances in laser technology have made these agents less invasive with lower complication rates such as prolonged catheterization, bacteruria, and urethral strictures. Compared to the time-tested TURP, laser ablation is costlier. However several studies indicate that the quality of life improvement is comparable to that achieved with TURP.

- Endoscopic resection
Transurethral prostatic resection is hailed as the gold standard of surgical treatment of bothersome BPH and symptomatic BOO that interferes and/or reduces quality of life.

It is an endoscopic modality that allows for circumferential resection of hypertrophied tissue with concomitant fulguration for hemostasis. An additional advantage of the standard TURP is the acquisition of prostatic tissue or chips. This allows for a true tissue diagnosis of BPH. If there is concern for malignancy, prostatic chips will allow for pathological confirmation.

- Open surgery
Open suprapubic prostatectomy is an invasive option that is reserved for men with large, greater than 100-g prostates that would otherwise require multiple, staged endoscopic procedures.

References


