Men Have Bladders, Too

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14.1 Introduction: It Is Not Always the Prostate

For most of the history of urology, particularly since the introduction of the resectoscope and the transurethral resection of the prostate, it has been assumed that prostatic enlargement, obstruction, and infection were the causes of essentially all lower urinary tract problems in men. It is now obvious that this is not the case. Bladder problems of all types are prevalent in men, generally to a similar degree found in women. Yet men continue to be misdiagnosed, underdiagnosed, mistreated, and undertreated. This may be due in part to residual prejudices in the medical community, but it also relates to reluctance of men to discuss these problems. A great deal of research has documented the stigma of urinary incontinence and how this makes patients reluctant to seek treatment. It is likely that this is magnified for men. At a Simon Foundation Innovating for Continence meeting, a female member of a patient panel reported how relieved she was that adult continence products were placed next to the menstrual pads. Needless to say, this does not provide any shelter to the man with incontinence.

Doctors need to ask all patients, men and women, about their bladder function and be prepared to offer evaluation and treatment. Despite decades of effort at patient education (and some success), the majority of those suffering with bladder disorders remain reluctant to seek help.

What Makes a Normal Bladder? Since lower urinary tract function is rarely taught in medical training, a few words about normal function should precede the discussion of abnormal conditions. The functional classification system detailed

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below was developed decades ago by Alan Wein; it remains the best way to think about lower urinary tract function and dysfunction [1].

Relevant Anatomy The lower urinary tract is conveniently considered to be simply composed of the bladder and the bladder outlet. The urinary bladder has a protective inner transitional cell lining (to prevent absorption of the excreted urine) covered by three layers of smooth muscle. It contracts under parasympathetic stimulation through the pelvic nerve. Relaxation during filling is facilitated by β-adrenergic stimulation via the hypogastric nerve.

In the male, the bladder outlet consists of the bladder neck (internal sphincter), the urethra, the prostate, and the external sphincter. The bladder neck is also composed of smooth muscle, but its primary receptors are α-adrenergic which facilitate closure; the external sphincter is composed of striated muscle and is under somatic control through the pudendal nerve. The primary neurotransmitter is norepinephrine. However, in classification, it helps to initially consider the entire bladder outlet as a single unit.

Overview of Function The normal lower urinary tract has two roles: urine storage and bladder emptying. In order to store urine properly, three things must be present:

1. The bladder must hold urine at low pressure and with appropriate sensation.
2. There must be no involuntary bladder contractions.
3. The bladder outlet must be closed at rest and remain closed against abdominal pressure.

Similarly, emptying is dependent on three basic factors:

1. There must be a coordinated bladder contraction of adequate magnitude and duration.
2. The outlet must open in coordination with the bladder contraction.
3. There cannot be any fixed anatomic obstruction.

All lower urinary tract dysfunction can be attributed to failure of one (or more) of these six properties.

Classification of Lower Urinary Tract Dysfunction Lower urinary tract dysfunctions can thus be classified as *failure to store* (broadly, incontinence) and *failure to empty* (broadly, retention). Furthermore, the dysfunction can either be *because of the bladder* or *because of the outlet*. This leads to a simple Wein classification system (Table 14.1); for example, one type of failure to empty because of the outlet is

Table 14. 1 Classification of lower urinary tract dysfunction

	Failure to store (incontinence)	Failure to empty (retention)
Because of the bladder	Overactive bladder, urgency incontinence, interstitial cystitis	Atonic/hypotonic bladder (e.g., diabetes, sacral injury, peripheral neuropathy)
Because of the outlet	Stress incontinence	Benign prostatic obstruction, sphincter dyssynergia, urethral stricture

urinary retention in males due to enlarged, obstructing prostate. The advantage of this system is that it is intuitive and each classification leads to a potential treatment algorithm. The disadvantage is that patients may have more than one dysfunction combining to produce very complex clinical problems (a woman with impaired bladder contractility and sensation due to diabetes who also has involuntary bladder contractions and stress incontinence).

The Basic Evaluation Sophisticated testing is rarely indicated in the initial evaluation of lower urinary tract symptoms. The essential elements of the work-up are the history, physical exam, urinalysis, post-void residual, and frequency-volume chart (bladder diary). Attention should always be paid to the reversible causes of LUTD as defined in the DIAPPERS mnemonic by Dr. Neil Resnick in 1985 (delirium, infection of urine, atrophic vaginitis, pharmaceuticals, psychological disorders/depression, excessive urine output, restricted mobility, stool impaction).

History As always, a complete history is essential in the evaluation of lower urinary tract dysfunction. However, there are a few items of particular importance to consider in the history.

- Define the problem: Understand the primary complaint, categorize as storage or emptying, and think about the possible problems noted above. However, regardless of the primary complaint, always ask about other lower urinary tract symptoms (LUTS); if complaint is leakage of urine, make sure to define emptying function and vice versa. Ask about urinary tract pain and gross hematuria.
- Onset: Most lower urinary tract problems have a slow, chronic onset. When the onset is abrupt, urinary tract infection must always be considered as a possibility. Acute and subacute onset often suggests a specific, reversible etiology.
- Past medical history: Any neurologic disease, and particularly low back disease, should be considered as a specific cause of lower urinary tract symptoms.
- Medications: A great many medications have anticholinergic properties and thus may affect bladder function. The cumulative effect of multiple anticholinergics is often underestimated.
- Review of symptoms: The colorectal, sexual, and neurologic review of symptoms is particularly relevant to complaints of lower urinary tract disease (LUTD) and should always be included.

Physical Exam A good urologic exam need not take a long time but it does require that patients undress. As patients often mention urinary and sexual problems right at the end of a visit, it is often inconvenient to perform a proper physical examination. In such cases, it is useful to suggest that the patient keep a home bladder diary (see below) to better quantify the LUT function and return for an exam and discussion of the problem. The exam should include a percussion/palpation of the bladder after voiding (reasonably accurate in slender patients to exclude significant urinary retention), resting anal sphincter tone, force and coordination of voluntary sphincter contraction, size and consistency of the prostate, and a basic assessment of sacral sensation (perianal and pedal).

The Bladder Diary The most underutilized tool in the evaluation of LUTD is the bladder diary or frequency-volume chart. The patient simply records the time and volume of each urination for 24–48 h. It is critical to record individual nighttime voids. Other information such as fluid intake, time and cause of incontinent episodes, degree of urgency, and degree of pain all may be helpful, but the key is to understand the typical function of the specific patient. While there is published normative data that is inadequate, consider these guidelines in counseling patients:

- Healthy 24-h urine output: 1500–2500 cm^3 (more urine output puts more stress on the bladder, but we want our patients to be adequately hydrated for overall health)
- Average single urination: 8 oz/1 cup/240 mL
- Maximum single urination: 12–20 oz/2 cups/360–600 mL (almost always the first morning void or a void that wakens the patient from sleep)

Combined with validated symptoms scores, the bladder diary is an important tool to assess a patient's progress over time and response to specific therapies.

Residual Urine As noted above, bladder percussion/palpation can be used to assess residual urine in slender patients. As ultrasound technology becomes less expensive, simple bladder scanners may become practical for primary care groups. Catheterized residual checks are highly accurate but much less acceptable in men than in women and should be avoided unless it is critical to obtain a sterile urine specimen.

14.2 Abnormal Bladders

Overactivity: The Overactive Bladder (OAB) OAB is a symptom syndrome (also urgency-frequency syndrome) defined as "urgency, with or without urge incontinence, usually with frequency and nocturia" occurring in the absence of infection or other proven pathology [2]. The cardinal symptom is urgency, "the complaint of a sudden, compelling desire to pass urine, which is difficult to defer" [2]. The primary point of the syndrome name is to include patients who suffer from urinary urgency but do not have incontinence. It is a syndrome, likely composed of several different subgroups which are yet to be defined. The definition implies an underlying pathophysiology of involuntary bladder contractions, but these are seen in only about 50 % of OAB patients during urodynamic testing. Of course, it is composed of a broad spectrum, but it is emphasized that the condition should be bothersome and that frequent urination alone (without urinary urgency) is not enough to assign this diagnosis.

Epidemiology No urologic diagnosis (with the possible exception of erectile dysfunction) has entered the public eye to the degree of OAB. The vast majority of the research and patient education efforts have been directed toward women; this likely

makes men less aware of the abnormality and less likely to seek treatment. Nevertheless, epidemiologic studies make it clear that OAB is common in men.

OAB is typically divided into "wet" (with urgency incontinence) and "dry" (without urgency incontinence). While OAB is very common in men, OAB wet is relatively uncommon. For both men and women, OAB is common in all ethnic groups studied and is the prevalence correlates with age.

In a US population-based telephone survey, the prevalence of OAB in women was approximately 30 % for all racial groups, whereas the prevalence in men ranged from 15 % in US whites to 18 % in Hispanics and 20 % for African-Americans [2]. The same study found the prevalence of urgency incontinence to be 6–10 % among men but 15–19 % among women. If a stricter definition is used for OAB (symptoms occurring a few times a month as opposed to "sometimes"), the prevalence falls to 10–15 % in women and 4–6 % in men, still very significant numbers. The symptom burden falls heavily on older men. The prevalence increased steadily by decade of life but accelerates markedly after age 50. The specific problem of OAB in elderly men has been nicely reviewed by Griebling [3].

A study designed to model the worldwide prevalence of lower urinary tract disease from existing data estimates an increase in males with OAB from 205 million in 2008 to 247 million in 2018; similar estimates for women were 250 million and 299 million, respectively. While more common in women, it is clear that OAB is not simply a female disorder.

Etiology: Obstruction vs. Idiopathic? As noted in the introduction, all LUTS in men have traditionally been assumed to be due to benign prostatic obstruction (BPO). There is, of course, an underlying rationale for this—animal models of partial bladder outlet obstruction are among the most commonly used to study OAB, isolated storage symptoms are much less common in men than in women, and OAB symptoms are observed to resolve in the majority of men who undergo surgical relief of obstruction. However, OAB without obstruction also occurs in men—both as a primary problem and as persistence of storage symptoms after relief of obstruction.

The etiology of idiopathic OAB is still unknown and most probably will ultimately be determined to be due to different causes in different patient populations. Postulated causes include urothelial dysfunction, myogenic dysfunction, and occult neurologic (central or peripheral) dysfunction. There is some theoretical and basic science evidence to support each of these, but at this time, there is no agreed-upon means to stratify OAB patients into these criteria, and we are not currently able to determine how our treatments might be optimized by identifying specific phenotypes [4].

Diagnosis The basic approach to diagnosis has been stated—history, physical examination, frequency-volume chart, urinalysis, and post-void residual. In male OAB patients, the primary distinction that needs to be made initially is whether the OAB symptoms occur in the context of significant emptying symptoms (or elevated residual urine) or if the storage symptoms occur in isolation.

Additional testing that may be considered:

- Urinary flow rate/PVR: A normal urinary flow rate and low residual are highly predictive of normal voiding dynamics; BOO is largely excluded. However, a low urinary flow rate argues against pure OAB but does not provide a clear diagnosis; it could be due to either BOO or detrusor underactivity.
- Pressure-flow urodynamics: Pressure-flow urodynamics are the "gold standard" in understanding lower urinary tract dysfunction. Bladder outlet obstruction can be definitively diagnosed as can normal voiding. While data remain inadequate, it appears that patients with documented bladder outlet obstruction have a better outcome with surgical therapy and are less likely to respond to treatment for OAB than those who are not obstructed. When BOO is excluded, treatment options aimed at the bladder are more attractive. However, many patients fall into an equivocal or indeterminate classification where optimal management is uncertain.
- Cystoscopy: Cystoscopy is useful for patients who are considering surgical therapy as the size and configuration of the prostate influences surgical decision making. There is, however, no utility for cystoscopy in diagnosing BOO or OAB.
- Imaging: Upper tract imaging is not indicated in the evaluation of lower urinary tract symptoms (but may be indicated for specific findings such as hematuria or a markedly elevated PVR). Prostate sizing by ultrasound may be useful if surgery is contemplated, and the digital rectal exam is felt to be inadequate to estimate size.

For those interested in more detailed information, the updated American Urologic Association OAB Guidelines and the European Association of Urology 2015 Guidelines are recommended [5, 6].

Treatment Treatment of OAB in men remains controversial. If there are any emptying symptoms whatsoever, the treatment algorithm will follow that outlined in the BPH chapter (INSERT REFERENCE)—even when the storage symptoms clearly predominate. Sequential therapy (α-blocker first, followed by specific OAB therapy) is advocated in guidelines [7]. This discussion will focus on treatment of men with persistent OAB after treatment of BOO and those with monosymptomatic OAB. The AUA OAB Guidelines and Algorithm do not specify different therapies for male patients.

- Behavioral therapy: Substantial improvement in OAB can be obtained with simple means. Demonstrably effective, non-pharmacologic therapy includes:
  - Education. Changing behaviors begins with education about normal lower urinary tract function and about the condition; overactive bladder can be explained as an imbalance between bladder and sphincter activities. The bladder is overactive and this can be treated directly as explained below. However, improved urinary control can also come from improving sphincter function. In particular, learning to perform rapid contractions of the pelvic muscles or "quick flicks" when faced with urgency can abort the episode by activating a sacral inhibitory reflex.

  - Pelvic floor muscle training. Improving the strength and responsiveness of the pelvic floor is effective for all types of urinary incontinence.
  - Frequency-volume chart. A great deal of insight is also obtained by completing the FVC. Many patients identify problems—excessive fluid intake, urgency stimulated by caffeinated beverages, long delays between voids that lead to urgency episodes, etc. and begin to change behaviors without specific coaching.
  - Bladder training. A short voiding interval is selected based on the FVC, and patients are instructed to void at that time, regardless of the sense of urge. The goal is to dissociate normal voiding and urgency. The interval is gradually increased as continence and control are achieved.
  - Urge inhibition. Although less well studied, urge inhibition techniques are combined with quick flicks to allow the sense of urgency to pass, again dissociating normal voiding from urgency [8]. A study using cognitive behavioral therapy in children with refractory OAB showed very promising results. Superior results in older children suggest that such a program could be adapted to adult outpatient therapy.
- Pharmacotherapy: Anticholinergic (ACh) medications remain the first-line therapy for such men with OAB. Several clinical trials have examined ACh meds in OAB, either with or without α-blockers. It has long been recognized that studies of ACh monotherapy (against placebo) have shown good safety (no increase in acute urinary retention) even in the presence of documented bladder outlet obstruction [9]. It is less clear which men will benefit equally from monotherapy as compared to combination therapy with an α-blocker. One large RCT examining tamsulosin vs. solifenacin vs. combination therapy demonstrated improvement in all treatment arms against placebo with superiority of the combination arm in relief of urgency [10]. Then newest treatment for OAB, the β-3 agonist mirabegron, has also been demonstrated to be safe in the treatment of men with LUTS and BOO; clinical efficacy and optimal utilization are yet to be determined [11].
- Neuromodulation: Neuromodulation is an attractive option for men with refractory OAB when BOO has been ruled out. There is no risk of urinary retention with neuromodulation, and urethral instrumentation is avoided. There are two FDA-approved modalities for neuromodulation—percutaneous tibial nerve stimulation (PTNS) and InterStim sacral neuromodulation.
  - PTNS is delivered in an office setting with stimulation of the nerve through an acupuncture-type needle for 30 min, weekly × 12 weeks. It has been proven to be superior to sham therapy [12], to have equal efficacy and better tolerability than ACh (tolterodine) [13], and to have reasonably sustained long-term effect with maintenance therapy. Fifty patients who initially responded in randomized trials have been followed for 3 years [14]. Twenty-eight of 29 patients completing the follow-up maintained improvement for an overall response rate of 77 % while receiving an average of 1.1 treatments per month. The optimal utilization has yet to be determined. There is inadequate experience with male patients to know if there is any gender response bias.

Ideal candidates would seem to be patients who seek a non-pharmacologic solution and those who improve on ACh but are intolerant of the side effects.

  - InterStim: Approved by the FDA for the treatment of urinary urgency incontinence in 1997 and subsequently for urgency-frequency without incontinence in 1999, InterStim has been the mainstay of treatment for OAB patients who are refractory to pharmacologic therapy. It can be effective for even severe and complex cases. This device is permanently implanted, essentially a "bladder pacemaker." There is a test phase which can be performed in the office with a temporary external wire or in the operating room with an implanted electrode. In either case, the patient has an opportunity to evaluate the response before going on to the permanent generator implant. Surgery is generally performed under light sedation.
  - Approximately 2/3 of patients with refractory OAB respond to InterStim. Intermediate term results are good with one study showing mean 4-year responses of 70 % for urgency incontinence and 68 % for urgency-frequency [15]. Less than 20 % of the patients were male; this is similar to other published literature. Surgical reintervention remains common with an average of 1.7 procedures/patient in the 41 % who required additional surgery. The most common reasons for intervention were treatment failure (explantation) and lead repositioning. Infection, pain, need for MRI, and battery depletion are also reasons for reoperation. InterStim should be considered for patients with refractory OAB and reasonable life expectancy who are healthy enough to tolerate a surgical procedure.

- Botox injections: Botulinum toxin, officially named onabotulinumtoxinA to distinguish it from other botulinum toxin products, paralyzes muscle by blocking the release of acetylcholine at the neuromuscular junction. It cleaves SNAP-25, a protein receptor, so that the vesicles containing acetylcholine (and other neurotransmitters) cannot bind to the nerve terminal and release their contents. This is a reversible process with duration of effect lasting 2–6 months—seemingly longer in the bladder than in many other applications.
- InterStim presented a dramatic advance in treatment of refractory OAB, offering effective therapy to patients who previously only had the option of major surgery. Botox was approved by the FDA in 2013 and was even more of a game changer; patients could now be offered effective treatment in a 15-min office procedure under local anesthesia. However, Botox has some key differences that diminish its appeal—the procedure must be repeated over time, and the treatment can be "too effective" leading to urinary retention.
- It is not possible to define gender differences in response to Botox. The two multicenter registration trials leading to approval in the USA and Europe included over 1110 patients, only 135 of whom were men [16, 17]. As only half of these were actually randomized to receive Botox, the numbers are simply too small to draw conclusions. The overall data show marked improvement in incontinence and urinary urgency episodes with Botox. The global response rate (moderately or markedly improved) is 61 % with Botox compared to 29 % with placebo. Risks include urinary tract infection (difficult to analyze due to study definitions

but potentially as high as 24 %) and urinary retention. In the two trials, the percentages of patients who developed an increase in post-void residuals of ≥ 200 cm^3 were 8.7 and 8.8 % and 6.1–6.9 % initiated intermittent catheterization. Many studies have examined the long-term durability of injection therapy. It appears that it is uncommon to see loss of efficacy over time. The duration of response is typically 5–9 months, and the initial response predicts long-term results.

- While the bias is that men may be more likely to suffer urinary retention with Botox, the risk is probably very similar for well-selected patients with normal voiding dynamics. A more relevant issue for most men is the need for frequent instrumentation (typically every 6 months). Men are less accepting of this than women in an office setting, and a requirement for anesthetic makes the procedure extremely expensive over time.

Underactivity Detrusor underactivity (DUA) or hypocontractility is a poorly researched and poorly appreciated condition. There is not even a generally agreed definition. The International Continence Society proposed that detrusor underactivity was "a contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or failure to achieve complete bladder emptying within a normal time span" [18]. This definition lacks the specificity needed for clinical or epidemiologic research. The patients complain of weak and interrupted urine flow, straining, hesitancy, and a sense of incomplete emptying. Patients with DUA can also experience storage symptoms such as urgency and urge incontinence; Neil Resnick named this condition detrusor hyperactivity with impaired contractility and suggested that it was a common and unrecognized cause of urinary incontinence in the elderly [19]. An excellent literature review on this topic was presented by Osman and colleagues for those who are interested in further study [20].

Epidemiology It is certain that many men and women, particularly the elderly, are affected by DUA. However, there are no useful epidemiologic studies to understand how prevalent this condition may be. The barrier to doing epidemiologic studies is considerable as this is a urodynamically defined condition; the clinical symptoms are nonspecific, overlapping considerably with bladder outlet obstruction.

Etiology In men, there is an underlying assumption that poor emptying is due to bladder outlet obstruction and that poor emptying may persist after relief of obstruction due to DUA. Yet it is well known that many men with high-grade bladder outlet obstruction have been followed for years without deterioration in bladder function. The mechanisms by which obstruction results in DUA, why it occurs in one patient and not another, and how to clinically identify patients at risk are entirely unknown. Furthermore, it is certain that there are other etiologies for DUA; many older women are diagnosed with DUA who have no reasonable cause of obstruction. It is highly likely that this occurs in aging men, also. Many neurologic diseases can produce DUA, but these are generally classified as neurogenic bladder disorders and are discussed below.

Diagnosis The diagnosis of DUA requires a pressure-flow urodynamic study to determine the quality of the detrusor contraction. There are not yet adequate data to create specific diagnostic criteria. In general, patients with DUA have low-pressure contractions (≤20 cm H_2O), but in some cases, there is an initially adequate contraction that is poorly sustained. It has been suggested that a post-void residual of ≥40 % of the pre-void bladder volume could serve as a screen for potential DUA [6].

Treatment Treatment for DUA is rather unsatisfactory. Bethanechol is a cholinergic agonist that is approved for the treatment of acute postoperative and postpartum nonobstructive (functional) urinary retention and for neurogenic atony of the urinary bladder with retention. There is scant clinical evidence for its efficacy. In the author's experience, it may have some benefit for the patient with a large residual—perhaps emptying 50 % of bladder volume—but has no effect on patients in overt retention. Dosing is 25 to 50 mg TID to QID, and it is generally advisable to gradually titrate the dose upward as the expected cholinergic side effects (diarrhea, cramping, lacrimation, salivation, etc. are often problematic). A good outcome is tolerable side effects and enough improvement to obviate the need for catheterization.

Therefore, most treatment of DUA is focused on improving emptying. Alpha-blockers are accepted as first-line therapy for men with difficulty emptying—most studies of these drugs obviously include men with DUA as pressure-flow urodynamics are rarely used in clinical trials and symptoms cannot differentiate DUA from true bladder outlet obstruction. DUA is perhaps more easily recognized/accepted in women; one study from Taiwan of women with "chronic, bothersome voiding symptoms" treated all patients with 0.2 mg tamsulosin (half of the FDA-approved dose for men in the USA). They found that the response rate (defined as moderate to marked improvement in symptoms) was 66.6 % for those diagnosed with BOO compared to 50 % for those with DUA. Similar nonstatistically significant trends toward a better response in BOO were seen for objective measures, but it certainly seems that DUA patients can respond to α-blockers. There is no indication that any one of the approved drugs is superior in this patient population.

Only one study investigated combination therapy for DUA. Yamanishi and colleagues randomized 119 patients with DUA to treatment an α-blocker, a cholinergic agent, or both [21]. Various outcome measures clearly favored combination therapy. For the subgroup of men, there was statistically and clinically significant improvement in total symptom score (measured by IPSS) with combination and with α-blocker alone but not with the cholinergic.

The diagnosis of DUA is particularly important and controversial when symptoms are refractory or post-void residual becomes worrisomely high (particularly if ≥ the voided volume). There is no doubt that some of these patients will respond to surgical intervention and sometimes even a second operation. However, there have been a great many men over the years that have been subjected to multiple prostate operations with diminishing results and ultimately end up on intermittent catheterization because the underlying problem was DUA not BOO. There is at least general agreement that pressure-flow urodynamic studies are appropriate for:

- Men with chronic or large-volume urinary retention
- Men with LUTS who are still voiding but have very large residual urine (usually considered > 250 cm^3)
- Men with persistent LUTS after surgical intervention

If preoperative studies indicate DUA, this does not mean that surgery is inappropriate; rather, the patient should be counseled about a lower likelihood of successful outcome and offered the option of intermittent catheterization.

Of course, the ultimate intervention for DUA is intermittent self-catheterization (ISC). While many men are unable to accept this, it can dramatically improve quality of life. New hydrophilic catheters significantly diminish discomfort. Catheter supplies fit easily into a "belly bag" or briefcase and can be used in almost any public restroom. The difference between taking 2 min to catheterize 3–5×/day and straining to empty a failing bladder 15–20 times/day can be dramatic. The primary complications are transient discomfort, occasional mild hematuria, and urinary tract infections. Most men on ISC may have 1–2 episodes of simple cystitis per year which are easily treated. It is important to realize that these men will always have bacteriuria, and no effort should be made to treat this unless there are clear symptoms of infection (pain, frequency, etc.).

Bladder Pain If bladder problems are already decidedly "unmanly," there is little doubt that bladder pain is very difficult for men to acknowledge. Not surprisingly, there is essentially no research into this problem as it applies to men. Bladder pain conditions are currently grouped as bladder pain syndrome/interstitial cystitis (BPS/IC). These patients present with urinary frequency and urgency that is driven by increasing pain with bladder filling. However, interstitial cystitis (IC) is best considered as a distinct condition. It is characterized by discrete flat, erythematous lesions that are visualized at cystoscopy and demonstrate severe acute and chronic inflammation on biopsy. In contrast, bladder pain syndrome (BPS) is defined by the American Urologic Association and the Society for Urodynamics and Female Urology as "An unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder, associated with lower urinary tract symptoms of more than 6 weeks duration, in the absence of infection or other identifiable causes" [22]. While the symptoms are identical, these patients have normal appearing bladders at cystoscopy, and biopsies do not show inflammation [23].

Epidemiology It was commonly thought that only about 10 % of patients with BPS/IC were male. Only two published clinical studies specifically report on the occurrence of BPS/IC in men. Both are single-institution, retrospective chart reviews and tell us nothing about the overall epidemiology. Novicki and colleagues identified 29 men diagnosed at the Mayo Clinic over 8 years, 86 % of whom were previously diagnosed with prostatitis or BPH [24]. These were older patients (average 67.3 years) and 70 % had ulcers. Similarly, Forrest and Vo found that 83 % of their 52 male patients were referred with diagnoses of chronic prostatitis, BPH, or epididymitis [25]. On the other hand, their average age was only 44 years, and only 10 % of their patients had bladder ulcers. They also reported a female to male ratio in

their practice was 7.6:1. There is nothing in either paper to suggest that male patients have a different clinical course or behave differently in response to treatment than do women.

The thinking that BPS/IC is uncommon in men has been recently challenged. The National Institutes of Diabetes, Digestive, and Kidney Diseases sponsored a nationwide, population-based survey on the prevalence of bladder pain symptoms. The Rand Interstitial Cystitis Epidemiology (RICE) developed case definitions of disease that could be ascertained by phone interview, validated them on a subset of responders who were willing to come in for an in-person evaluation, and then performed the nationwide survey. The results were surprising to many. In adult women, the prevalence estimates for BPS/IC range from a possible high of 6.53 % using a high-sensitivity definition to a low of 2.7 % using a high-specificity definition [26]. Only 10 % of those surveyed had actually been diagnosed with BPS/IC. When the same group performed a population-based screen in men, they found that the comparable prevalence estimates for BPS/IC were 4.2 % to 1.9 %—much closer to that of women than most expected [27]. In addition, they found that 1.8 % of men met a single high-sensitivity/high-specificity case definition for chronic pelvic pain syndrome (CPPS). The overlap between these two groups was only 17 %. It is clear from this study that

- BPS/IC is common in the male population; the female to male ratio is about 3:2.
- There may be as many (or more) men with BPS/IC as the more commonly diagnosed CPPS.
- Pelvic pain syndrome is an enormous problem for adult males.

Etiology Little is known about the etiology of BPS/IC. The most widely discussed theory, lower urinary dysfunctional epithelium (LUDE), is on the wane as there is no reliable test for this condition, and only a minority of patients respond to specific treatment with pentosanpolysulfate or heparin, and recent studies show no dose response to a nearly tenfold increase in pentosanpolysulfate dosage. Promising basic science work that detected a specific protein (antiproliferative factor) in BPS/IC patients urine that inhibits bladder epithelial growth has also disappointed. The protein has been fully identified, but the work has not been reproduced in other labs, and there is as yet no clinically useful test for the protein nor any treatment.

It is the feeling of the author (and many others) that while IC is a specific condition and may well ultimately be shown to have a clear etiology, BPS is really a syndrome that is best considered the common expression of different identifiable phenotypes [28]. It is likely that we will one day be able to identify a specific BPS bladder phenotype, and it may well be due to a urothelial abnormality. However, the most common phenotype may well be due to myofascial pain/pelvic floor dysfunction. Here, both the bladder pain and lower urinary tract symptoms are actually initiated by myofascial trigger points in the abdomen and pelvis in combination with poor relaxation/coordination of the pelvic floor muscles. Pudendal neuralgia can produce symptoms that mimic BPS/IC, and it is likely that other phenotypes can be described that respond to specific therapies. Finally, it is important to recognize that

many patients with urologic chronic pelvic pain syndromes have significant comorbid systemic pain syndromes such as fibromyalgia [29]. This represents an important phenotype in which it is not always wise to focus on the pelvic pain.

Diagnosis Guidelines for the diagnosis of BPS/IC have been published by the American Urological Association, including an algorithm for evaluation and treatment [30]. The basic evaluation for all patients includes a history and physical examination, frequency-volume chart, determination of post-void residual, urinalysis, urine culture, and use of validated instruments to assess overall symptoms and pain. Urine cytology is recommended if there is a smoking history. The presence of hematuria or pyuria in the urinalysis should prompt a cystoscopic examination (as well as upper tract imaging). Other studies are usually not helpful. In men, an important consideration is bladder outlet obstruction due to prostatic enlargement or bladder neck dysfunction. Therefore, the post-void residual is an important screening test, and pressure-flow urodynamics should be considered if this is elevated or there are significant bladder emptying symptoms. In all cases, the need for additional diagnostic testing should be reassessed if the patient does not respond well to treatment.

Treatment The AUA Guidelines treatment algorithm describes six levels of treatment beginning with education and behavioral therapies and ending (in rare patients) with cystectomy and reconstruction or urinary diversion. There is also a detailed discussion of the principles of treatment; it is critical to properly evaluate each treatment modality, optimize successful treatments, and avoid polypharmacy. There is little if any evidence that men with BPS/IC respond differently to treatments than women, but some perspectives on the common treatment modalities are presented:

- Oral medications: Pentosanpolysulfate, amitriptyline, cimetidine, and hydroxyzine are all presented as acceptable second-line treatments. While amitriptyline is arguably the single most effective medication for bladder pain, the prominent anticholinergic side effects of this drug (and the anticholinergics indicated for overactive bladder which are also commonly used in this condition) can aggravate/expose any difficulty in emptying. The antihistaminic effects of hydroxyzine can do the same. This issue may be more of a problem for male patients.
- Intravesical therapies: A variety of intravesical "cocktails" using dimethyl sulfoxide or some combination of pentosanpolysulfate or heparin with local anesthetic agents have been employed in BPS/IC. Patients who respond can often be taught to perform home instillations as part of the chronic therapy. Men may be more reluctant to accept catheterization, but newer hydrophilic catheters ease this discomfort, and these therapies should not be discouraged.
- Hydrodistention under anesthesia: Some have argued that ulcerative IC is more common in men. While this cannot be demonstrated, an endoscopic examination to look for ulcers should certainly be performed whenever a patient is not responding to therapy.

The author has argued that we have typically been too passive in our approach to BPS/IC therapy, willing to settle for any improvement. In "An Oncologic Approach to UCPPS" [31], the idea of working to normalize bladder capacity and eliminate all symptoms when possible is proposed as a means of allowing the sensitized nervous system to revert back to normal achieving a sustainable complete remission. It is important to follow the patient's frequency-volume chart and symptom scores and understand to what degree symptoms are still present when the patient reports improvement.

14.2.1 Neurogenic Bladder

Overview Neurogenic bladder (NGB) is one of the least useful and most misused terms in urology. It can appropriately be defined as any lower urinary tract dysfunction that occurs in a patient with a neurologic disorder that could reasonably be attributed to that disorder. In truth, we are rarely able to prove that a neurologic disease is the proximate cause of LUTS; we can simply note that the time courses of the two conditions are parallel and that the neurologic condition is the most likely source of the symptoms.

Common neurogenic disorders and lower urinary tract outcome:

- Stoke: The cerebral edema of acute stroke often produces detrusor areflexia and urinary retention. This almost always resolves as the patient recovers unless there is massive injury. Stoke patients always have coordinated voiding and typically empty well so men with persistent retention after stroke should be investigated for bladder outlet obstruction. The most common long-term problem in stroke patients is overactive bladder (properly referred to here as neurogenic detrusor overactivity) with urge incontinence. The likelihood of persistent OAB after stroke is related to the severity of the injury/greater cerebral damage. These patients are much more likely to have incontinence without sensation (in contrast to typical urgency incontinence) than neurologically intact individuals.
- Multiple sclerosis: The unfortunate fact about multiple sclerosis (MS) is that lower urinary tract manifestations are as varied as the disease itself. The most common manifestation of MS is overactive bladder, but it is very common that these patients suffer from combined storage and emptying problems. Although upper urinary tract complications are uncommon with MS, they are more likely to occur in men; male patients deserve closer monitoring.
- Parkinson's disease: It is widely recognized that LUTS are common in patients with PD. Parkinson's disease (PD) has been an area of considerable controversy in urology; the most common manifestation is detrusor overactivity, but there may also be emptying dysfunction due to poor relaxation of the urinary sphincter. It has long been argued that men with LUTS and PD were poor candidates for surgical therapy because of the high prevalence of DO that would persist after surgery. However, current thinking is simply that it is important to make an

accurate diagnosis. A small study of men and women presenting for treatment of PD who were willing to undergo pressure-flow urodynamic testing found that 75 % had detrusor overactivity and only 14 % had bladder outlet obstruction (enlarged prostate was an exclusion criteria). Not surprisingly, men were more likely to be obstructed. If clear prostatic obstruction is present (and particularly if there is also increased post-void residual urine), surgery should not be denied.

- Spinal cord injury: The most serious NGB disorder is spinal cord injury (SCI) and the related myelomeningocele. These disorders are much more likely to lead to upper tract complications including renal failure. As with stroke, there is a period of spinal shock in the acute injury phase. As this resolves, the ultimate pattern takes shape. The type of LUTD in complete injury is largely predictable by the level of injury, but this is not true with incomplete injuries. Sacral injuries destroy both the sacral micturition center and the connection to the cortical micturition center leading to urinary retention. Suprasacral lesions allow the sacral micturition center to function without cortical inhibition and produce detrusor overactivity and incontinence. Lesions above T6 are the most serious as the coordination of urination is also affected. There is detrusor overactivity with external sphincter dyssynergia; these patients are at a particularly high risk for upper tract complications and deserve the closest monitoring.
- Radical pelvic surgery: Surgery for pelvic cancers, particularly radical hysterectomy and colectomy, presents a risk for bladder denervation and urinary retention. In male patients, this may lead to a prostatectomy with disastrous results. The bladder may actually be areflexic but noncompliant leading to severe urinary incontinence after TURP. Thoughtful evaluation and high-quality pressure-flow urodynamic evaluation are mandatory for these patients.

Management Principles In the same way that "neurogenic bladder" is a very nonspecific term, the management of patients with NGB must be individualized. Important considerations include:

- The natural history of the neurologic disease. Is progression likely? Will it impact the LUTD? Will it impact the patient's ability to manage the LUTD (make it to the toilet when faced with urgency, perform self-catheterization).
- The risk of upper urinary tract complications. When urodynamic studies show high pressures during storage (common in spinal cord injury and sometimes seen in MS), there is a clear risk of upper urinary tract damage over time. Monitoring is mandatory, and intervention may be required even when symptoms are not severe.
- The overall condition of the patient. It is common that NGB patients may have multiple disabilities and some of these (cognitive impairment, limited mobility, limited hand function) may impact management.

Each patient deserves careful evaluation and an individualized plan for both monitoring and treatment.

Nocturia Nocturia is the most bothersome lower urinary tract symptom and often the reason that men seek treatment. It is, unfortunately, the least likely to respond to standard therapy. Despite this, little research had been done on this problem until recent years. Our knowledge of nocturia is substantially improved by new knowledge. We understand that nocturia is most commonly not due to the bladder and that the lack of treatment response is indicative of not identifying the underlying cause. Nocturia is easy to evaluate, many effective interventions exist once properly classified, and it is best managed by the primary care physician.

Epidemiology The ICS defines nocturia as "the complaint that the individual has to wake at night one or more times to void" [2]. The individual must wake from sleep and return to sleep after voiding. Nocturia increases steadily with age and the point at which nocturia becomes abnormal and/or bothersome is not totally clear; most clinical research includes only subjects with a minimum of two episodes of nocturia.

Nocturia is clearly age related. An excellent literature review (recommended reading for those interested in the subject) by Bosch and Weiss found that "men in their 20s and 30s, 11 % to 35.2 % reported at least 1 void per night while 2 % to 16.6 % reported 2 or more voids nightly. Of men in their 70s and 80s, 68.9 % to 93 % reported at least 1 void per night while 29 % to 59.3 % reported at least 2 voids per night" [32]. The authors note that nocturia is much more common in younger women (perhaps due to sleep issues, responsibilities with children, etc.), but in older individuals, the gender difference disappears. There is no indication at this time that race or ethnicity contributes to nocturia.

Differential Diagnosis and Evaluation Strategy The basic diagnostic tools for all bladder conditions—history, physical examination, frequency-volume chart (FVC), urinalysis, and post-void residual determination—suffice in nearly all cases where nocturia is the chief complaint. It is important to know the medical history since so many conditions can cause nocturia. The history generally allows for classification of nocturia as an isolated condition (no daytime complaints) or as part of a global LUTS. The presence of snoring or other related nighttime issues can suggest sleep apnea or other sleep disturbances. On the physical exam, it is critical to look for peripheral edema, one of the most common and treatable causes of nocturia. The FVC is, however, indispensable as the cornerstone of effective diagnosis and management of nocturia.

The FVC must record the volume of all voids for at least 24 h (preferably 2–3 days) and the hours of sleep. While "normal" is necessarily a range, the FVC allows the clinician to analyze urine production and bladder function together. Some basic calculations are used to classify nocturia:

- 24-h urine production. This enables the diagnosis of global polyuria which is suspected with urine outputs >2500 cm^3 or 40 cm^3/kg.
- The percentage of urine produced during sleep. Nocturnal urine output includes the first morning void. This enables the diagnosis of nocturnal polyuria—generally defined as >33 % of urine made during sleep hours—a lower percentage for younger patients. 90 cm^3/h of sleep has also been suggested [33].

Table 14.2 Classification of lower urinary tract dysfunction

Classification of nocturia by frequency-volume chart	
Findings on FVC	Suggested etiologies
Low bladder volumes day and night	Lower urinary tract dysfunction—OAB, BPO, BPS/IC
Low bladder volumes night only	Sleep disorder
Nocturnal polyuria	Peripheral edema, CHF, behavioral issues
Global polyuria	Behavioral issues/polydipsia, uncontrolled diabetes, etc.

- Daytime/nighttime average and maximum void volumes. Lower volumes (average voids <200 cm^3, maximum voids <300 cm^3) identify patients who may have underlying lower urinary tract dysfunction).

This classification provides the insights needed to look for correctable/treatable causes of nocturia (Table 14.2). Proper treatment depends on proper classification. Nocturia is often multifactorial, and the initial management is typically focused on optimizing medical conditions such as CHF and peripheral edema. Diuretics can be used at in the late afternoon when compression stockings and elevation of the feet are insufficient to manage the edema. Treatments aimed at the bladder are usually only successful when nocturia is part of a day and night symptom complex; these should be reserved for those who have such a diagnosis. Sleep disorders can be identified and treated.

Desmopressin is a medication which is specifically approved for nocturnal enuresis in children. It is a synthetic analog of vasopressin that temporarily decreases urine production. It has been shown to be effective in adults [34] although it has not yet gained FDA approval for this indication. A common starting dose is 50 mcg and the drug can be titrated to 400 mcg. Patients should be monitored for hyponatremia, particularly the elderly. There is some evidence that men are less sensitive to the effects of desmopressin and may require higher doses.

14.3 Summary

Bladder problems are common in men, in many cases with similar frequency to that found in women. In most cases, men respond well to the same treatments that are effective for women so the primary challenge is in identifying and diagnosing these conditions. The primary care physician can do this effectively in the majority of cases and call for urologic consultation whenever the diagnosis is in doubt or the patient fails to respond to appropriate therapy.

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