

Lower urinary tract symptoms and benign prostatic hyperplasia

Old problems, new solutions

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Benign prostatic hyperplasia is a common cause of lower urinary tract symptoms (LUTS). Newer medications and minimally invasive treatments are now available in Australia, although the long-term outcomes are as yet unknown. Common questions asked by GPs and patients are answered here.

Lower urinary tract symptoms (LUTS) affect millions of men in Australia. The most common cause of LUTS in Australian men is benign prostatic hyperplasia (BPH). This article highlights some of the key aspects in the management of men with LUTS due

to BPH, including:

- important steps in the work-up of patients with LUTS
- 'red flag' symptoms indicating that early referral to a urologist is warranted
- baseline investigations to conduct in primary care

KEY POINTS

- One in five men over the age of 35 years are bothered by lower urinary tract symptoms (LUTS).
- The most common cause of LUTS is benign prostatic hyperplasia (BPH).
- In a patient with LUTS, there are certain 'red flag' clinical features for which early urological referral is recommended.
- There are many options for medical therapy of men with LUTS and the choice of drug should be individualised after a thorough assessment has been conducted.
- Although transurethral resection of the prostate (TURP) remains the gold standard for surgical treatment of men with BPH, newer minimally invasive procedures are available with fewer side effects. However, the long-term durabilities of these procedures are still being determined.

MedicineToday 2016; 17(11): 14-25

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1. SYMPTOM CLASSIFICATION OF LOWER URINARY TRACT SYMPTOMS IN MEN

Voiding (obstructive) symptoms

- Weak stream
- Poor flow
- Intermittency
- Post-micturition dribbling
- Hesitancy

Storage (overactive) symptoms

- Nocturia
- Urgency
- Frequency

Red flag symptoms*

- Haematuria
- Incontinence (urge/overflow especially at night)
- Urinary retention
- Recurrent urinary tract infections
- Bladder calculi
- Renal impairment
- Hydronephrosis

* If present, referral of the patient to a urologist is strongly recommended.

useful to determine the degree of both the various BPH symptoms are causing a patient. It helps to predict which patients may benefit from treatment and also to monitor their response to therapy. It may also be used to prompt the clinician to assess important aspects of LUTS.

How prevalent are LUTS?

In a recent Australian study of men aged between 35 and 80 years, it was found that one in five men have bothersome LUTS.² As age increases, the prevalence of bothersome LUTS increases, with more than 60% of men aged 60 to 69 years old being affected. 'Bothersome' is defined by a score of more than eight on the I-PSS (moderately or severely symptomatic).

Are LUTS associated with prostate cancer?

There are several causes of LUTS (Box 2), with BPH being the most common. However, many patients who present with LUTS

- the newer medical and minimally invasive surgical therapies available in Australia.

The article is written in a question and answer format. The questions are based on common questions the authors have been asked in their daily practice by both patients and GPs.

What are common LUTS?

Depending on how BPH affects the urinary tract, different symptoms may develop. These may be voiding or storage symptoms or a combination of both (Box 1).

The International Prostate Symptom Score (I-PSS) is a useful tool for clinicians (Table 1).¹ This validated questionnaire is

TABLE 1. INTERNATIONAL PROSTATE SYMPTOM SCORE (I-PSS)¹

Questions about urinary symptoms*	Not at all	Less than 1 in 5 times	Less than half the time	About half the time	More than half the time	Almost always	Your score
In the past month, how often have you had the feeling of not completely emptying your bladder?	0	1	2	3	4	5	
In the past month, how often have you had to urinate again within the next two hours?	0	1	2	3	4	5	
In the past month, how often have you stopped and started again several times when urinating?	0	1	2	3	4	5	
In the past month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5	
In the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5	
In the past month, how often have you had to strain to begin urination?	0	1	2	3	4	5	
Question about nocturia*	None	1 time	2 times	3 times	4 times	5 times	Your score
In the past month, how many times per night did you typically get up to urinate?	0	1	2	3	4	5	
Total I-PSS score[†]							
Question about quality of life due to urinary symptoms [‡]	Delighted	Pleased	Mostly satisfied	Mixed	Mostly dissatisfied	Unhappy	Terrible
If you were to spend the rest of your life with your urinary symptoms the way it is now, how would you feel about that?	0	1	2	3	4	5	6

* The I-PSS is calculated from the answers to seven questions about urinary symptoms including nocturia.

[†] Score: 1 to 7 = mildly symptomatic; 8 to 19 = moderately symptomatic; 20 to 35 = severely symptomatic.

[‡] The International Scientific Committee recommends the use of one question to assess the quality of life. This may serve as a valuable starting point for a doctor-patient conversation.

do so because they are concerned about prostate cancer. Patients can be reassured that having LUTS does not increase their risk of prostate cancer compared with asymptomatic men.^{3,4}

A simple illustration is useful in explaining to men that BPH generally affects the periurethral part of the prostate gland, therefore causing LUTS (Figures 1a and b). On the other hand, most prostate cancer originates in the peripheral part of the prostate gland, away from the urethra, and therefore most men with prostate cancer are

asymptomatic. This is a useful strategy to help patients understand the difference.

What tests should a GP consider ordering in a patient with LUTS?

The various tests a GP should consider ordering in the primary care setting are outlined in Table 2.

A voiding diary filled out by the patient for two or three consecutive days can help to delineate and objectively assess the degree of frequency, incontinence and fluid intake. An example of a diary is available

at www.continence.org.au/resources.php/01tA0000001b1c2IAA/bladder-diary.

Examination of the patient's prostate gland is controversial in general practice. However, we suggest, at the very least, an examination of the patient's foreskin, if present, to exclude phimosis as the cause of symptoms.⁵

When should a patient be referred to a urologist?

There are absolute and relative indications for when to refer a patient with LUTS to a

urologist (Box 3). The absolute indications or complications of BPH generally require the patient to undergo some form of urological intervention (Figure 2).

The relative indications are those that place patients at higher risk of developing complications or indicate a need for specialised investigations.

What type of tests may a urologist order?

After taking a comprehensive patient history, and conducting an examination and baseline tests (as in Table 2), the underlying aetiology, severity and acuity of the LUTS can usually be determined. When a patient is reviewed by a urologist, several other specialised tests can be arranged if necessary, as outlined below.

A voiding flow study

The authors advocate liberal use of voiding flow studies where available. This five-minute test is performed in the clinic in association with a post-void residual bladder scan. It can help to determine if obstruction is present, the type of obstruction (i.e. bladder outlet versus urethral stricture) and the post-void residual volume. The results can be used as a baseline measurement for assessing a patient's response to therapy.

Urodynamics

A urodynamic study is a test that usually takes about 45 minutes and can be performed in an outpatient setting. Most patients do not need a urodynamic study. It is indicated in patients who are suspected of having a neurogenic cause for their LUTS, to assess bladder function and integrity, or to determine more accurately the degree of bladder outlet obstruction.

Urethrocytoscopy

A urethrocytoscopy (commonly known as a 'cystoscopy') is a minimally invasive procedure that can be performed under local anaesthetic. It is not routinely used in the work-up of patients with LUTS but can be useful to determine the presence of a stricture or bladder abnormalities or

to investigate haematuria. Some procedures to treat men with BPH are better suited to certain sized prostates and prostate size is best determined with a urethrocytoscopy.

Which medication should be prescribed first in patients with LUTS?

Medical therapy is indicated in patients with LUTS who have:

- bothersome symptoms (usually I-PSS >8)
- failed conservative measures, including
 - fluid management, such as caffeine moderation, restricting alcohol intake and limiting intake of fluids in the evening
 - behavioural therapy
 - timing of medication, such as not taking diuretics in the evening in patients with nocturia
 - treating constipation
- no complicating features necessitating referral of the patient to a urologist (Box 3).

Table 3 lists drugs commonly used to treat men with LUTS. Awareness of the key differences between the various drug classes helps in determining which medication is best suited to a particular patient.

2. CAUSES OF LOWER URINARY TRACT SYMPTOMS (LUTS)*

Most prevalent symptoms

- Benign prostatic obstruction
- Overactive bladder–detrusor overactivity
- Nocturnal polyuria

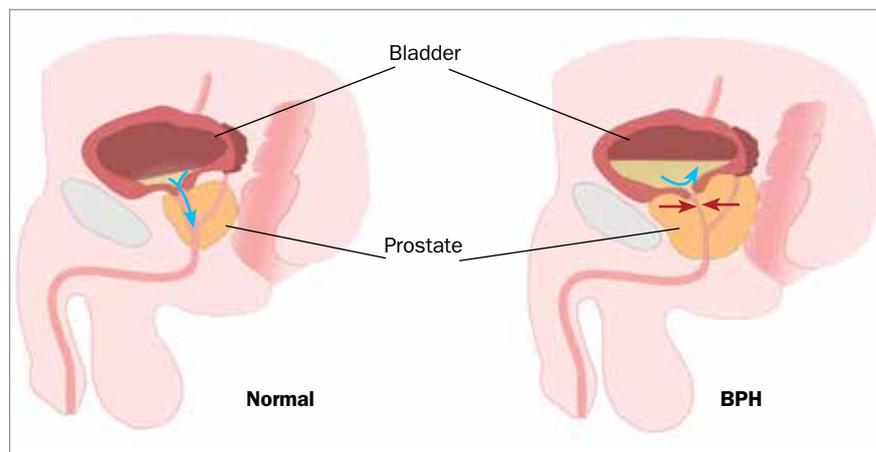
Other symptoms

- Detrusor underactivity
- Neurogenic bladder dysfunction
- Urinary tract infection
- Prostate cancer
- Distal ureteral stone
- Prostatitis
- Urethral stricture
- Bladder tumour
- Foreign body

* It is common for more than one of these factors to be present in men with LUTS.

Given that different classes of drugs target different LUTS, some patients respond better to a combination of drugs from different classes rather than using separate drugs in isolation.

In general, the authors tend to prescribe tamsulosin 400 µg/day as a first-line medication for men with LUTS. This is a well-tolerated medication with few side effects and has a convenient once daily



Figures 1a and b. Anatomy of a normal prostate (a, left) and an enlarged prostate with benign prostatic hyperplasia (b, right). The urethra is narrowed in men with BPH (red arrows) and the flow of urine is disrupted (blue arrows).

3. INDICATIONS FOR REFERRAL OF A PATIENT WITH LUTS TO A UROLOGIST

Absolute indications

- Haematuria
- Renal impairment
- Urinary retention
- Bladder calculus
- Hydronephrosis
- Recurrent urinary tract infections

Relative indications

- Raised prostate specific antigen level
- Urinary incontinence
- Severe symptoms (I-PSS >20)
- Failure to respond to first-line therapy
- Raised post-void residual volume of more than 100 mL
- Past history of urinary retention
- Neurogenic aetiology
- Unclear diagnosis

Abbreviations: I-PSS = International Prostate Symptom Score; LUTS = lower urinary tract symptoms.

dosage (Table 3). However, it is currently only available on the PBS as a Repatriation Schedule of Pharmaceutical Benefits (RPBS) item for Department of Veterans' Affairs beneficiaries; the cost for other affected men is about \$60 per month.

A combined formulation of dutasteride

TABLE 2. TESTS TO CONSIDER IN A PATIENT WITH LOWER URINARY TRACT SYMPTOMS

Test	To investigate for
Urinalysis/midstream urine	Infection
Blood glucose	Diabetes
Creatinine, urea, electrolytes	Renal impairment
Ultrasound kidney/ureter/bladder	Post-void residual volume, bladder lesions/calculi, hydronephrosis
Prostate specific antigen*	Prostate cancer

* Should be performed after informed consent has been obtained and generally for patients 40 to 70 years old.

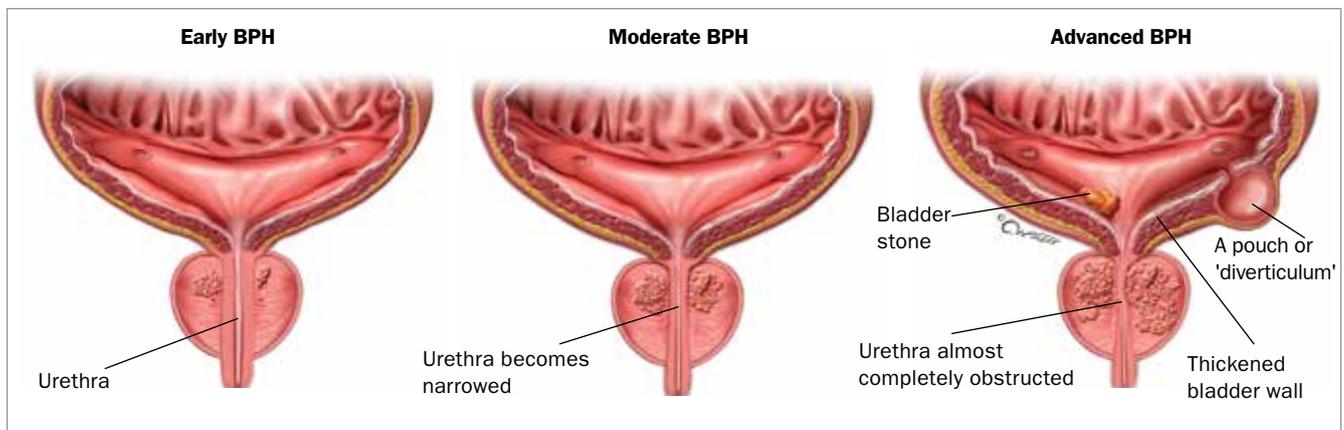
and tamsulosin is available and covered by the PBS. This drug is better suited for men with larger prostates (>30 g) but the patient needs to be informed that dutasteride, and therefore this combination medication, can cause sexual dysfunction, including low libido, that may be permanent even after discontinuation of the medication.

Mirabegron and tadalafil have recently been shown to be efficacious in men with LUTS.⁶ Mirabegron is an agonist of the beta 3-adrenoceptors that when activated induce relaxation during the storage phase of the micturition cycle. Therefore, for patients who have specific storage symptoms, as outlined in Box 1, this drug may be of benefit. As it does not affect the

voiding phase of micturition, it does not increase the risk of urinary retention.⁷ This is one of the major advantages of the beta 3-adrenoceptors over the anti-muscarinics, which have traditionally been used to treat men with overactive bladder-type symptoms. Furthermore, although there are no large comparative trials, mirabegron seems to be better tolerated than the antimuscarinics in terms of side effects.

Tadalafil 5 mg/day has been shown in a large meta-analysis to improve LUTS in men with BPH.⁸ Therefore, it is useful in men with coexisting LUTS and erectile dysfunction.

The authors occasionally prescribe mirabegron or tadalafil as first-line



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Figure 2. Complications of benign prostatic hyperplasia, including progressive narrowing of the urethra, bladder stones, pouch development and thickened bladder wall.

TABLE 3. COMMONLY PRESCRIBED DRUGS FOR MEN WITH LOWER URINARY TRACT SYMPTOMS

Drug class	Generic drug name	PBS listing for BPH or LUTS	Best suited for	Key notes	Main side effects
Alpha blockers	Alfuzosin	Yes, on the RPBS with authority	Men with small prostates (<30 g)	May still be used in men with larger prostates Tamsulosin, a once daily medication, is better tolerated than prazosin, which has a twice daily dosage	Postural hypotension Reduced ejaculate volume/retrograde ejaculation
	Prazosin	No			
	Tamsulosin	Yes, on the RPBS with authority			
5-Alpha reductase inhibitors combined with alpha blocker	Dutasteride and tamsulosin	Yes, with authority	Men with larger prostates (>30 g)	The dutasteride component shrinks the prostate over 3 to 6 months	As for alpha blockers plus Reduced libido (may be permanent) Erectile dysfunction
Antimuscarinics	Darifenacin	No	Men with overactive bladder-type symptoms	May be combined with alpha blockers Caution if raised PVR Oxybutynin available as transdermal patch (change twice weekly)	Dry mouth Dry eyes Constipation Urinary retention Memory impairment
	Oxybutynin	Yes, with restricted benefit			
	Solifenacin	No			
	Tolterodine	No			
Beta 3-adrenoceptor agonists	Mirabegron	No	Men with overactive bladder-type symptoms	May be combined with alpha blockers May be used in patients with raised PVR	Hypertension Nasopharyngitis Headache
Phosphodiesterase type 5 inhibitors	Tadalafil	Yes, on the RPBS with authority for erectile dysfunction	Men with mild LUTS and erectile dysfunction	5 mg per day May be combined with other BPH medications	Headache Dyspepsia Myalgia Nasopharyngitis

Abbreviations: BPH = benign prostatic hyperplasia; LUTS = lower urinary tract symptoms; RPBS = Repatriation Pharmaceutical Benefit Scheme; PVR = post-void residual volume.

medications if certain symptoms predominate, as discussed above.

There is no evidence that herbal remedies significantly improve LUTS.⁹

When should a patient be considered for surgery?

A surgical de-obstructive type procedure should be considered in patients who:

- have complications of BPH as outlined above
- want to cease medical therapy due to:
 - failure to respond
 - side effects
 - costs
 - not wanting ‘life-long’ medication.

Are there any new surgical options for men with BPH?

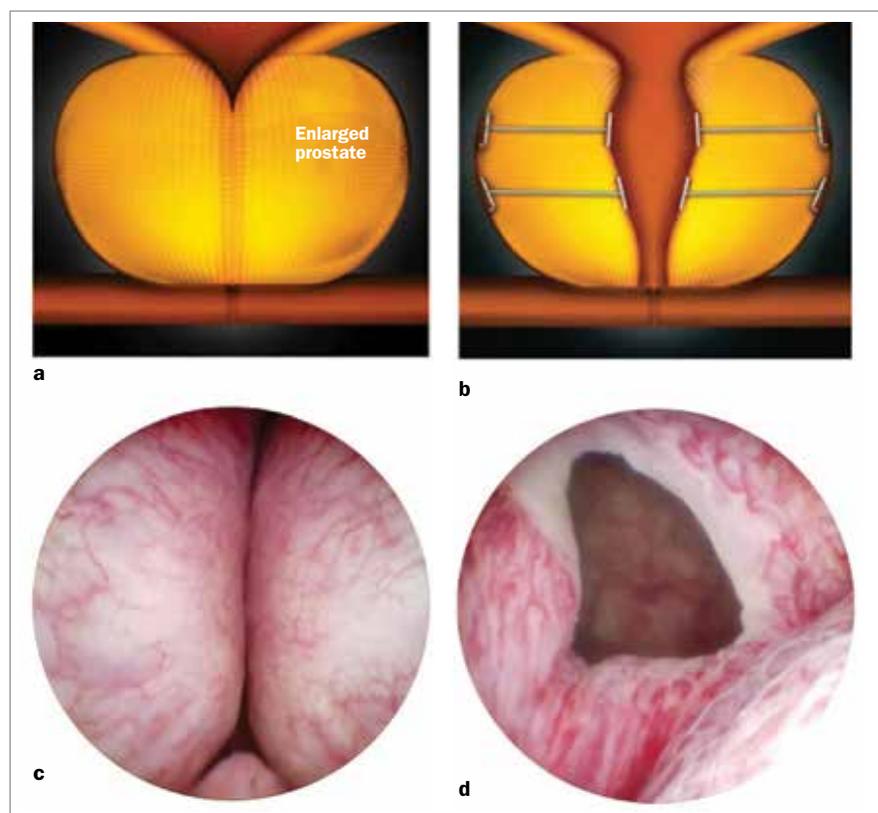
Although discussing with patients the detailed differences between the surgical options for BPH is outside the scope of practice for most GPs, it is important they understand the general principles and indications for the various de-obstructive procedures available. This becomes increasingly so as new procedures with niche indications are developed and patients become aware of their availability before seeing a urologist.

Until recently, the surgical options most commonly used in Australia for men with BPH were cavitating treatments. These include transurethral resection of the

prostate (TURP), Greenlight laser vaporisation, laser enucleation and open simple prostatectomy. In terms of improvement in I-PSS and durability, TURP is still used as the gold standard comparator in most studies.

Although the cavitating treatments are effective, they universally share a common side effect in most patients – that is, retrograde ejaculation. This side effect can be very bothersome and may result in the avoiding of surgery by some patients who may otherwise benefit from a procedure.

In 2012, the Therapeutic Goods Administration approved the Urolift® System. To date there have been more than 2000 Urolift® operations performed in Australia.



Figures 3a to d. Urolift® procedure. a and c(left). Before the procedure. b and d (right). After. Images courtesy of Dr Darren J Katz.

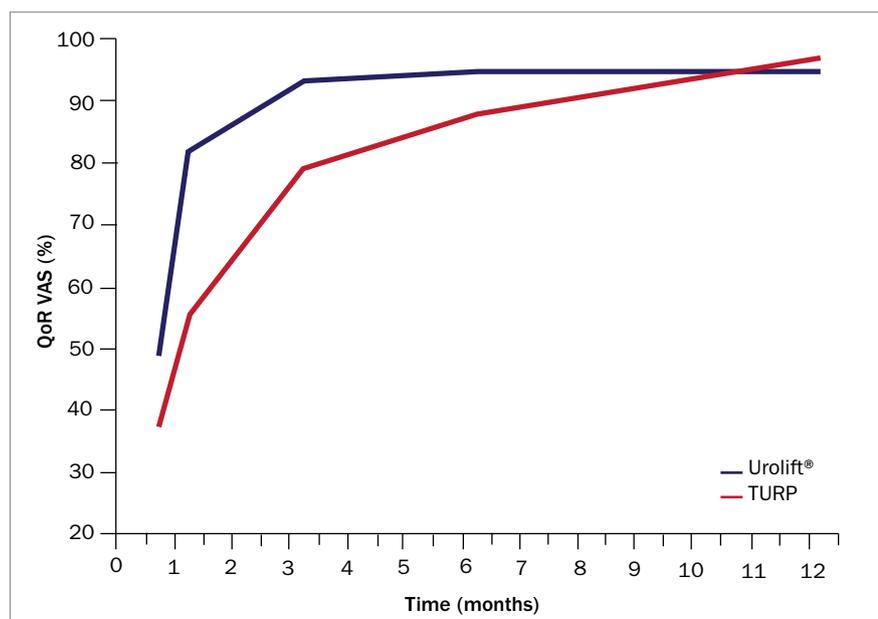


Figure 4. Recovery after surgery for benign prostatic hyperplasia. Percentage of subjects reporting 70% or more on the visual analogue scale for quality of recovery (QoR VAS) after prostatic urethral lift (Urolift®) and transurethral resection of the prostate (TURP) treatment.¹²

The benefit of this procedure is that there are no reported sexual side effects and it can be performed as a day case without need for a catheter.¹⁰ The Urolift® procedure involves placement of several retractors into the prostatic lobes to increase the urethral opening (Figures 3a and b).

The side effects of the Urolift® procedure may include dysuria, frequency, urgency and pelvic discomfort, although most are mild to moderate and resolve within two to four weeks. However, not all prostates are suitable for the Urolift® procedure (i.e. men with prostates >80 g or with large protuberant median lobes) and the durability of the procedure has only been published to four years.¹¹ The re-operation rate in this time period is 13%.

Although having a high satisfaction rate, the Urolift® procedure does not improve the I-PSS and peak flow as much as the gold standard operation, TURP. However, patients seem to recover quicker from the Urolift® procedure compared with TURP. The patients who describe having a 'high-quality recovery' by one month was 82% from Urolift® procedure compared with 53% for TURP.¹² However, by 12 months, both procedures had similar high-quality recovery rates (Figure 4).

TURP can have significant side effects, including urethral stricture (7%), clot retention (5%), urinary tract infections (UTIs; 4%), need for blood transfusion (3%) and TURP syndrome (1%).¹³ TURP syndrome can be avoided by performing the TURP using bipolar technology, which allows saline to be used as an irrigation solution. The re-operation rate of TURP is about 10%. If tissue is required for histology, then a TURP is the only procedure that can be used to provide this.

Patients taking anticoagulants can be a challenging group for surgery. In patients who are unable to cease anticoagulants or antiplatelet agents, Greenlight laser vaporisation or laser enucleation can be performed with limited risk of bleeding.¹⁴ For some surgeons, Greenlight laser vaporisation is now the procedure of choice for some patients regardless of anticoagulant status.

For men with very large prostates (>120 g), laser enucleation or open prostatectomy can be used.

How can a patient be optimised perioperatively?

Before any type of surgical procedure on the urinary tract it is important to ensure that a patient has sterile urine. If possible, it is best to cease use of antiplatelet agents and anticoagulants and allow the drugs to be cleared before the procedure is performed. Restarting these medications should be done in consultation with the treating urologist. However, as mentioned above, some procedures can be performed while patients continue to take these drugs. Ensuring patients are not experiencing significant constipation before surgery can also help their postoperative recovery.

During the operation, most patients are given some form of intravenous antibiotic prophylaxis. Most patients do not need any antibiotics after the procedure.

For several reasons, patients often experience an exacerbation of their storage symptoms after a de-obstructive procedure has been performed. This usually settles without therapy but can sometimes persist for weeks or even months. In such cases, a short-term trial of medications such as mirabegron or an antimuscurinic can be helpful. Although some of these symptoms may mimic a UTI, in most cases a urine test will be sterile (although pyuria and microhaematuria will be present as a result of the surgery), and antibiotics are not indicated.

Conclusion

The medical and surgical treatments for men with BPH continue to evolve. A comprehensive work-up of the patient is essential to identify which patients need referral to a urologist and will also help to target therapy. Although some newer procedures have fewer side effects than traditional surgery, the long-term outcomes are not yet known. **MT**

References

A list of references is included in the website version of this article (www.medicinetoday.com.au).

COMPETING INTERESTS: None.

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