Benign Prostatic Hyperplasia

Benign prostatic enlargement, BPH

The term *benign prostatic hypertrophy* is also used but technically it is incorrect. Hypertrophy means enlargement of the components without an increase in their numbers as happens with muscle fibres. Hyperplasia is an increase in the number of the components and this is typical of glandular enlargement.

**Description**

Benign prostatic hyperplasia (BPH) is an increase in size of the prostate gland without malignancy present and it is so common as to be normal with advancing age. It seems likely that the nature of BPH is a failure of apoptosis (natural programmed death of cells) and that some of the drugs used to treat it may induce that process.[1]

The prostate secretes about 20-30% of the volume of seminal fluid. It is a hormone-dependent gland and BPH does not occur in castrated men.

It should be borne in mind that lower urinary tract symptoms (LUTS) and BPH are not synonymous. Prevailing European guidelines suggest that because BPH is so common in older men, it should not be looked on as the only possible pathology in patients presenting with LUTS. The doctor assessing a patient with LUTS should take an holistic view bearing in mind the full range of causes and the possibility of co-existing morbidities.[2]

**Epidemiology**

BPH affects the quality of life of about 40% of men in their fifth decade and 90% of men in their ninth decade.[2] It is unusual before the age of 45 and affects men of Afro-American origin more severely than white men, possibly due to higher testosterone levels, 5-alpha-reductase activity, androgen receptor expression and growth factor activity. One study found some correlation between LUTS and increased prostate volume.[3] Another study found that the mean length of prostate increased faster than the height and width, especially after the age of 60 years. The transitional zone volume and transitional zone length had a higher correlation with the International Prostate Symptom Score (IPSS) than total prostate volume.[4] The prostate increases in size with passing years but at a decelerating rate. Between the ages of 31 and 50 it doubles in size every 4.5 years but this rate reduces subsequently.[5]

**History**

History should focus on a number of specific features that are typical of the disease. This should be followed by the IPSS to give an assessment of the effect on the quality of life. If surgery seems likely (and bearing in mind the age of most men who present with this condition) further questions to assess fitness for surgery may be in order.

- **Urinary frequency** is often a presenting symptom. Ask how many times a day he needs to void and how often he has to rise at night. Ask also if he passes small or large volumes of urine each time. When enquiring about urinary frequency, it is necessary to distinguish frequent passage of small volumes from polyuria. To this end it may be helpful to complete a frequency/volume chart.
- **Urinary urgency** may occur and manifests as a need to pass urine quickly for fear of incontinence.
- **Hesitancy** occurs when he has to stand at the toilet for a while before he can initiate micturition. There is usually a poor stream and dribbling of urine too and he may stop during the act.
- **Incomplete bladder emptying** gives the sensation of still having urine in the bladder, no matter how often he goes. He may even be able to pass more immediately after he has finished.
- There may be a need to **push or strain**, increasing the risk of micturition syncope.
The IPSS is a quantitative and validated technique based on eight questions and a further quality-of-life question. The results are summated to give a figure for the degree of trouble caused by the condition. The IPSS is free for the use of individual clinicians and non-funded research.[6] The results are scored and severity of the symptoms is classified according to the score:

<table>
<thead>
<tr>
<th>Interpretation of IPSS score</th>
<th>Score</th>
<th>Classification</th>
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<tbody>
<tr>
<td></td>
<td>0-7</td>
<td>Mild symptoms</td>
</tr>
<tr>
<td></td>
<td>8-19</td>
<td>Moderate symptoms</td>
</tr>
<tr>
<td></td>
<td>20-35</td>
<td>Severe symptoms</td>
</tr>
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Examination

- Examination of the abdomen includes checking for a palpable bladder. This may indicate chronic outflow obstruction or a neurogenic bladder. To exclude the latter, an enquiry about motor or sensory loss along with checking knee and ankle jerks and plantar responses should suffice. Obviously, any further abnormalities require a full neurological history and examination.
- Digital rectal examination (DRE) includes noting the tone of the anal sphincter and the pelvic floor. It may be poor with a neurogenic bladder. The size of the prostate is assessed. Urologists report their findings in terms of the size of the prostate, a normal gland in a young adult weighing about 20 g. A useful guide for those less familiar with prostates is that a finger’s breadth represents about 15 to 20 g and so a gland that is three fingers in breadth across is 45 to 60 g. Symptoms are unusual below two fingers in breadth. It is also important to note the texture and contour of the gland. It should be firm but not hard, and smooth without nodules. The median sulcus should be clearly defined. A gland that is hard rather than firm, nodular and lacks a clear median sulcus suggests carcinoma of prostate.
- If an elderly person is likely to need surgery, a brief check of the cardiovascular and respiratory systems is also needed.

Investigation

Urine
Check urine by dipstick and send MSU for microscopy and culture.

Blood
- Routine blood tests include:
  - U&E and creatinine
  - FBC
  - LFTs

Abnormal LFTs may indicate other disease. Isolated elevation of alkaline phosphatase can occur:
- If the prostate is malignant and has metastasised to bone.
- In an elderly person, where it may represent undiagnosed Paget’s disease of bone.

- PSA is elevated with a large, benign prostate. Experts consider that gentle DRE is unlikely to raise the PSA result. A combination of clinical examination and PSA levels may be a better way of attempting to differentiate between a benign and malignant prostate, although evidence to support this may be lacking.[7] It should be recognised that normal PSA values change with age: [8]
### PSA Cut-off Values

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>PSA Cut-off</th>
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<tbody>
<tr>
<td>40-49</td>
<td>2.0 nanogram/mL or higher</td>
</tr>
<tr>
<td>50-59</td>
<td>3.0 nanogram/mL or higher</td>
</tr>
<tr>
<td>60-69</td>
<td>4.0 nanogram/mL or higher</td>
</tr>
<tr>
<td>70 or older</td>
<td>5.0 nanogram/mL or higher</td>
</tr>
</tbody>
</table>

There are no age-specific reference limits for men older than 80 years of age.

Patients (and sometimes doctors) expect a test to give a simple affirmative or negative answer and so a booklet to help understand the PSA test may be of value. A high result may occur in benign disease and may be associated with an increased risk of having LUTS requiring treatment.\[9\]

### Imaging

Imaging may also be necessary if there is any suggestion of urinary tract obstruction.\[10\]

Ultrasound examination of the prostate may be used prior to surgery or if it will assist choice of medical therapy.

### Other investigations

- The European Association of Urology suggests that post-void residual bladder volume should be part of any routine assessment of male LUTS.\[2\] It can be estimated by passing a catheter and measuring the volume but ultrasound is comfortable, non-invasive and accurate. This is only currently recommended as part of specialist assessment by the National Institute for Health and Care Excellence (NICE).\[11\]
- Further investigations that may possibly be required include assessment of urine flow rate. It should be used as a baseline before embarking on any treatment, whether medical or surgical. The maximal flow rate (Qmax) is the single best measurement but a low Qmax does not help to differentiate between obstruction and poor bladder contractility. More detailed analysis requires a pressure flow study. A Qmax value over 15 mL/second is usually considered normal. A Qmax below 7 mL/second is accepted as low. Results can vary according to effort and volume and so the usual compromise is to obtain at least two readings with at least 150 mL of urine each time.
- Pressure studies are rather invasive but may be necessary if there is suspected bladder neck obstruction. A voiding pressure above 60 cm water with a Qmax of under 15 mL/second is regarded as diagnostic.
- Endoscopy may be required. A flexible cystoscope can be used as an outpatient procedure with a topical anaesthetic gel. It takes several minutes and may be useful if urethral stricture is suspected. This may follow prolonged indwelling catheter or gonococcal urethritis. It may also be used if a lesion in the bladder is suspected.

### Differential diagnosis

- Bladder tumours
- Bladder stones
- Bladder trauma
- Chronic pelvic pain
- Chronic prostatitis
- Detrusor instability
- Interstitial cystitis
- Neurogenic bladder
- Prostate cancer
- Radiation cystitis
- Urethral strictures
- Urinary tract infection (UTI)
Management\textsuperscript{[2, 12, 13]}

See also separate Lower Urinary Tract Symptoms in Men article.

- If symptoms are minimal, ‘watchful waiting’ (WW) is the most judicious option, provided that malignancy has been excluded.\textsuperscript{[14]} One study found that WW was more readily used by specialist than by primary care physicians.\textsuperscript{[15]} The three key components which seem to contribute to the effectiveness of this approach are reassurance, education and monitoring.
- Other management does not always have to be surgical and there are several drugs which have proved useful to control the condition and they have been reviewed.
- A trial of medical therapy may still be followed by surgery, if required.
- Irrespective of the mode of management chosen after discussion with the patient, there should be periodic follow-up to assess progress, as the natural history is a tendency for symptoms to worsen.
- Complications, as discussed at the end, may necessitate referral, even as an emergency.
- There is some evidence supporting the use of lifestyle advice along with other modalities of treatment. BPH has been related to factors such as obesity and thus it is probably good to counsel patients on healthy diet regimens and involvement in exercise programmes if possible.\textsuperscript{[16]}

Drugs

- Alpha-adrenergic antagonists, or alpha-blockers, reduce the tone in the muscle of the neck of the bladder. They should be offered to men with moderate-to-severe voiding symptoms (corresponding to an IPSS of 8 or more). There are alpha-1 receptors that are subdivided into types 1a, 1b and 1c. The alpha-1a is predominant in the prostate, bladder neck and urethra and the most selective drug available is tamsulosin.\textsuperscript{[14]} Prescribers of tamsulosin should be aware of the existence of intra-operative floppy iris syndrome, a condition which causes the iris to ‘billow out’ during cataract surgery. This does not usually affect the long-term outcome but it can cause pain and prolong the recovery period. If warned, urologists can use techniques to minimise the risk of this occurring, so if GPs have prescribed tamsulosin, it is important for them to mention it in their referral letters.\textsuperscript{[17]}
- Less selective alpha-blockers include doxazosin, terazosin, prazosin, alfuzosin and indoramin. The less specific effects may sometimes be beneficial. For example, if the patient has BPH and hypertension, one drug may be beneficial for both.
- 5-alpha reductase inhibitor (5-ARI) drugs block the synthesis of dihydrotestosterone from testosterone and can reduce symptoms - eg, finasteride and dutasteride. They do work but it may take several months before benefit is noted. Unlike alpha-blockers, they have been shown to reduce the long-term risk (>1 year) of acute retention or need for surgery. They should be offered to men with LUTS and a prostate estimated to be larger than 30 g or PSA greater than 1.4 ng/mL and a high risk of progression.\textsuperscript{[13]} For patients with bothersome moderate-to-severe LUTS not responding to monotherapy and with a prostate estimated to be larger than 30 g or PSA greater than 1.4 ng/mL, consider an alpha-blocker plus a 5-ARI. Treatment should be continued for at least one year.
- There are a number of dietary supplements that are used in BPH. They are not available on FP10 but may be bought by the patient. Establishing an evidence base for the effectiveness of these products has been difficult due to variations in methodological techniques. One review of the literature reported some evidence for the effectiveness of beta-sitosterol, \textit{Pygeum africanum} and Cernilton\textsuperscript{®} but not for several other compounds.\textsuperscript{[18]}

Certain caveats should be observed:

- Avoid alpha-blockers in those with postural hypotension or micturition syncope.
- 5-ARIs may have an adverse effect on sexual performance and direct questioning about sexual history is needed. Problems include decreased libido, ejaculation disorder and erectile dysfunction, which may continue after the medication has been stopped. Generally, adverse effects are less than with alpha-blockers.
- Studies suggest that alpha-blockers continue to exert efficacy for at least four years.
- Due to their slow onset of action, 5-ARIs should be continued for many years.
**Surgery**

Surgery is usually reserved for those with a large prostate or failure to respond to an adequate trial of medical therapy.\(^{[2, 11]}\)

- Surgery is required if there is acute urinary retention, failed voiding trials, recurrent gross haematuria, UTI, renal insufficiency due to obstruction or failure of medical treatment.
- Open prostatectomy - transurethral vapourisation of the prostate (TUVP) is reserved for those with a prostate larger than 80 g, bladder stones or bladder diverticula and patients who cannot be positioned for transurethral surgery. The inner core of the prostate adenoma is shelled out, leaving the peripheral zone behind. There may be significant blood loss requiring transfusion. Open prostatectomy usually has excellent results in terms of improvement of urinary flow and urinary symptoms.
- Transurethral resection of the prostate (TURP) is now the standard technique. A working sheath is placed in the urethra through which a hand-held device with an attached wire loop is placed. A cutting diathermy is run through the loop so that it can be used to shave away prostatic tissue. When successful, it is an excellent operation that does not involve entering the abdomen but it can have complications. Bleeding may be difficult to control. Irrigating fluid may be absorbed into the circulation via cut veins. An indwelling catheter is required until bleeding has stopped. Urethral strictures can occur. There can be retrograde ejaculation after operation or damage to the nerves can cause erectile dysfunction.
- Insertion of prostatic urethral lift implants may be used when the man wishes to have a procedure with a lower risk of causing sexual dysfunction.\(^{[19]}\)
- Holmium laser enucleation of the prostate (HoLEP) is equally effective, has a lower morbidity rate and is being considered as first choice where available.
- Minimally invasive therapies usually involve heat destruction of prostatic tissue. Via the urethra, energy is transferred to destroy tissue, in the form of laser, microwaves, radiofrequency waves, high-intensity ultrasound and high-voltage electrical energy.
- Estimated prostate size smaller than 30 g: transurethral incision of the prostate (TUIP) or transurethral needle ablation (TUNA) can be offered as an alternative to TURP for patients wishing to avoid, or who are unfit for, more invasive surgery. Both treatments, however, have a higher recurrence rate than TURP. If the prostate size is larger than 80 g, this narrows the options to TURP, TUVP or HoLEP.
- It should be noted that surgical options are unlikely to be definitive procedures.
- Newer techniques such as prostate artery embolisation are being researched to assess safety and efficacy.\(^{[20]}\)

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**UroLift**

**Clinical Editor’s notes (July 2017)**

Dr Hayley Willacy notes that: the UroLift system is used to perform a prostatic urethral lift, a procedure that is an alternative to current standard surgical interventions such as transurethral resection of the prostate (TURP) and holmium laser enucleation (HoLEP).\(^{[21]}\) The UroLift system uses adjustable, permanent implants to pull excess prostatic tissue away so that it does not narrow or block the urethra. In this way, the device is designed to relieve symptoms of urinary outflow obstruction without cutting or removing tissue. NICE has concluded that the UroLift system is effective in relieving symptoms of benign prostatic hyperplasia - see reference below. It also noted that the degree of symptom relief outcomes is slightly less than that after transurethral resection of the prostate (TURP) or holmium laser enucleation (HoLEP), but it is sufficient and clinically important.

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**Complications**

Bladder outlet obstruction can result in:

- **Urinary retention**: this may be precipitated by anticholinergic drugs, including tricyclic antidepressants, opiates and diuretics.
- **Recurrent UTI**, especially with incomplete emptying.
- Impaired kidney function: progression to chronic kidney disease is much rarer now.
- **Bladder calculi** (may present as ongoing LUTS or recurrent infections).
- **Haematuria** - may be microscopic or macroscopic.
Patients on medical treatment should have symptoms assessed every six months. Every year PSA and DRE should be repeated. A benign prostate can undergo malignant change. In extreme old age, not only is BPH almost invariable but areas that seem to have at least carcinoma in situ are very common. This is probably best managed conservatively, as there is little evidence that an aggressive approach is beneficial.

## Indications for referral

NICE recommends referral for the following indications:[12]

- Acute retention of urine (admit immediately).
- Acute kidney injury (admit immediately).
- Visible haematuria (to be seen in two weeks).
- Suspicion of prostate cancer based on the finding of a nodular or firm prostate, or a raised PSA level, or both (to be seen in two weeks).
- Culture-negative dysuria (to be seen in two weeks).
- Chronic urinary retention with overflow or night-time incontinence (to be seen in two weeks).
- Recurrent UTI.
- Microscopic haematuria.
- Failure to respond to treatment in primary care with poor quality of life as assessed by the IPSS.

## Further reading & references


5. International Prostate Symptom Score; Urological Sciences Research Foundation
7. PSA measurements, frequently-asked questions; British Association of Urological Surgeons, March 2016
18. Insertion of prostatic urethral lift implants to treat lower urinary tract symptoms secondary to benign prostatic hyperplasia; NICE Interventional Procedure Guidance, January 2014
19. Prostate artery embolisation for benign prostatic hyperplasia; NICE Interventional Procedure Guidance, April 2013


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