

What is BPH?

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The prostate is located between the bladder outlet and pelvic floor. It surrounds the urethra and has functions in urinary continence and reproduction. Secretions of the prostate help to liquefy the ejaculate. Anatomically, the prostate can be divided into 'zones'(Chapter 11). BPH occurs predominantly in the transitional zone. The two primary histologic constituents of the prostate are glands and the fibromuscular stroma (the smooth muscle and connective tissue that occupy the space between glands). There is constant turnover of these components – just as there is a constant turnover of skin and many other body tissues. An imbalance in the cell renewal versus cell death with accumulation of glandular and stromal tissues results in benign prostatic hyperplasia (BPH). In contrast to prostate cancer, these glandular and fibromuscular components maintain normal differentiation and respect the natural boundaries of the prostate. These changes can be clinically detected as benign prostatic enlargement (BPE). The exact cause of BPH is unknown but is related to aging, genetic susceptibility, androgens, e.g., testosterone and dihydrotestosterone, estrogens and neurotransmitters.

The histologic findings in BPH are age-dependent and found in approximately 50% of men at age 50 and 90% at age 90. The clinical consequences of BPH are estimated to affect more than 16 million men in the US, making it the most common of all urological problems. Approximately 500,000 men per year in the United States undergo surgical therapy for BPH-related symptoms at a cost of over \$2 billion.

How does BPH cause symptoms and how is the diagnosis made?

In reviewing the clinical aspects of BPH, it is important to define the role of BPH in the pathophysiology of lower urinary tract symptoms (LUTS). BPH is a histologic rather than a clinical diagnosis. Consequently, while many men have histologic evidence of BPH, the number who have BPH-related LUTS (i.e., clinical BPH) is much smaller. Patients present because of LUTS, not BPE per se, and it is these symptoms that should be the primary focus in diagnosis and treatment.

The urethra passes through the center of the prostate and BPH can produce bladder outlet obstruction (BOO) by reducing the size of the lumen. Mechanistically, an increase in the 'bulk' of the prostate (glandular proliferation) or 'tightening' of the prostatic muscle (fibromuscular proliferation) can

occur. It is important to recognize that, (1) not all men with histologic BPH or BPE have clinical BPH, (2) clinical BPH can occur in the absence of marked BPE and (3) the degree of BPE does not predict the severity of LUTS and vice versa. Not all the symptoms of BPH are directly related to obstruction. Symptoms may be related to changes in the bladder occurring in response to obstruction (muscular hypertrophy and instability) or age-related changes.

While there are no universally accepted criteria for the diagnosis of clinical BPH, a diagnosis can often be made with history, physical exam and a few simple tests. Evaluation is directed towards determining if the symptoms or complications of BPH are present (i.e. urinary retention, infection, bleeding, bladder stone or renal failure) and also to exclude non-BPH conditions capable of producing similar symptoms.

Treatment is symptom-driven and therefore history is paramount. Use of the standardized American Urological Association symptom index (AUASI) is the single most useful tool to gauge symptoms. The 7 self-administered questions produce a score out of 35, with moderate and severe scores falling above 7 and 19, respectively. The AUASI is not specific for BPH LUTS but is useful in stratifying men for treatment in men who have clinical BPH.

Signs of the complications of BPH, prostate volume and any features suspicious for prostate cancer should be sought on physical exam. A urine analysis and PSA are the only tests routinely recommended by the AUA. In situations where the diagnosis is unclear, measurement of a post-void residual, urodynamics may be useful.

How is BPH treated?

Treatment is instituted in men with moderate or severe LUTS *and* who are bothered by them. The management of BPH has changed significantly over the past 20 years.

Surgical therapy is indicated in men who have moderate-severe clinical BPH in whom medical therapy has been unsatisfactory or men with a complication from BPH. Medical therapy is considered first line therapy in all other cases. Alpha-blockers and 5-alpha reductase inhibitors (5ARI) target the smooth muscle and glandular components of BPH, respectively. The alpha-1 receptor subtype is found in abundance within the prostate and bladder neck smooth muscle. Alpha-1 receptor blockade relaxes the muscle, but do not reduce prostate size. The commonly used alpha-blockers are terazosin, doxazosin, alfuzosin and tamsulosin. Alfuzosin and tamsulosin have the advantage of not requiring upward dose titration. Onset of action is rapid and they are proven to improve LUTS and flow rates. Side effects are uncommon and include hypotension, dizziness, weakness, and retrograde ejaculation. The 5ARI's, finasteride and dutasteride, address the glandular

component by the production of DHT (responsible for glandular growth) from testosterone. Prostate volume is reduced resulting in improved symptoms and flow rates over the course of several months. Side effects include breast enlargement and decreased ejaculatory volume. Alpha-blockers and 5ARI address the symptoms of BPH by different mechanisms. 'Combination therapy', the addition of 5ARI to an alpha blocker, has proven to be beneficial in men who have larger prostates and higher PSA's. In such patients, use of 5ARI's can decrease progression of symptoms and complications, such as urinary retention, whereas alpha-blockers do not prevent progression. For men who also have urgency, frequency and nocturia that are not a result of incomplete bladder emptying, anticholinergic medications (i.e. bladder relaxants) can safely be added to a treatment regimen.

The principle behind surgical therapy is to open the urinary passage by the removal or ablation of tissue. Surgery is usually done endoscopically through the urethra with no cutting of the skin. The transurethral resection of the prostate (TURP) is considered the gold standard for the surgical treatment of BPH. Innovation and evolution of surgical approaches is continuing at a high level and there are a wide variety of surgical procedures, each with variations. Other types of surgery utilize laser ablation or tissue destruction with heat or microwaves. Complications include bleeding, infection, incontinence, retrograde ejaculation and erectile dysfunction. The incidence of significant complications is low and the most severe complications are very infrequent. In general, the degree of improvement in AUASI, quality of life and flow rate are markedly higher with surgery than medication.

Summary

BPH is a common benign condition affecting the prostate that can produce bothersome urinary symptoms in men. Not all BPH causes symptoms and when urinary symptoms are present, obstruction of urinary outflow is but one mechanism. Evaluation with standardized symptoms scores, ascertainment of the effects on quality of life and a physical exam to exclude other conditions is important. BPH is caused by an imbalance in glandular and fibromuscular proliferation, both of which are addressed by the medical treatments of 5-alpha reductase inhibitors and alpha-blockers, respectively. When medical treatment fails or when a complication of BPH ensues, there are several highly effective minimally invasive surgical treatments available that continue to evolve with time.

Suggested reading

- Burnett AL, Wein AJ. Benign prostatic hyperplasia in primary care: what you need to know. *J Urol.* 2006; 175: S19-24.
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- Wilt TJ, N'Dow J. Benign prostatic hyperplasia. Part 1--diagnosis.*BMJ.* 2008; 336: 146-9.
- Wilt TJ, N'Dow J. Benign prostatic hyperplasia. Part 2--management.*BMJ.* 2008; 336: 206-10.