

## The Progression of Benign Prostatic Hyperplasia



Theresa J. McCallum, MD, FRCSC

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Benign prostatic hyperplasia (BPH) is a non-cancerous enlargement of the prostate caused by the growth of new cells. It results in varying degrees of bladder outlet obstruction. It is a progressive condition affecting men as they age. Most men do not experience symptoms until > 50-years-of-age; however, 80% to 90% of men > 80-years-of-age will describe voiding concerns.<sup>1</sup> The majority of patients can be managed by the primary care practitioner.

### *BPH etiology and androgen influences*

Prostate hyperplasia is probably due to an imbalance between cell proliferation and cell death. Hereditary factors dictate how large a prostate can potentially grow in each man. If a patient's relatives have had troubles from an enlarged prostate at a certain age then that patient may experience the same issues. Androgens can influence this potential and are involved in symptom control. Testosterone is converted to dihydrotestosterone (DHT) by the enzyme 5 $\alpha$ -reductase. DHT is the primary androgen responsible for accelerated growth of the prostate in BPH.

### *BPH symptoms*

An enlarged prostate compresses the urethra and, if large enough, may intrude into the bladder

### Quinn's case

Quinn, 77, presents in your office, unhappy with a daytime urination frequency of every 2 hours, nocturia 4-5 times a night, hesitancy, poor stream calibre and post-void dribbling. His coffee intake is 1.5 L q.d. He has longstanding hypertension and non-insulin dependant diabetes, but has poor compliance to his medication.

#### Physical

Physical findings include:

- Smaller stature
- BP: 166/98 mmHg
- Non-palpable bladder
- Digital rectal examination: moderate
- Benign, non-tender prostate

#### Labs

Laboratory findings include:

- Electrolytes normal
- Creatinine 120  $\mu$ mol/L
- Random glucose: 10.8 mmol/L
- Urinalysis clear
- PSA 7.6  $\mu$ g/mL

#### Initial plan

Your initial plan for Quinn is to decrease his coffee intake, control his diabetes and hypertension and start tamsulosin. You will also follow his PSAs.

**For more on Quinn, turn to page 70.**

itself. The bladder compensates to overcome this obstruction. Symptoms can be divided into problems of storage and/or problems with elimination (Table 1).

Table 1

## Benign prostatic hyperplasia (BPH) symptoms

Storage problems	Elimination problems
<ul style="list-style-type: none"> <li>• Urinary frequency</li> <li>• Urgency</li> <li>• Nocturia</li> <li>• Urge incontinence</li> <li>• Pain: perineal, suprapubic, abdominal, lower back</li> </ul>	<ul style="list-style-type: none"> <li>• Difficulty initiating stream</li> <li>• Weak urine stream</li> <li>• Straining to pass urine</li> <li>• Prolonged micturation</li> <li>• Involuntary post-void dribbling</li> <li>• Sensation of incomplete emptying</li> <li>• Acute or chronic urinary retention</li> <li>• Overflow incontinence</li> </ul>

### Natural history of BPH

The majority of men will have a worsening of voiding difficulties as they grow older. Over 50% will deteriorate, 30% may stay the same and 15%, surprisingly, may have improvement without therapies. If left untreated, BPH can progress to serious complications including:

- urinary retention requiring surgery,
- bladder decompensation (atony) and
- upper urinary tract compromise.<sup>2</sup>

As a man with symptoms ages, the risk of requiring BPH-related surgery increases. One-third of men > 70-years-of-age may need intervention.

The risk of poor voiding is increased with different medications, lifestyle and environmental variables<sup>2</sup> (Table 2).

### Diagnosing BPH

When diagnosing BPH, keep these factors in mind:

- Consider the severity of symptoms
- A urinary tract infection is suggested by rapid onset of symptoms
- Take note of tenderness on rectal exam and white blood cells on urinalysis
- Gross hematuria requires a prompt urologic referral
- Rule out cancer of the prostate by ordering a PSA

Table 2

## Voiding obstruction is increased with:

Medications	Lifestyle/ environmental variables
<ul style="list-style-type: none"> <li>• Antihistamines</li> <li>• Muscle relaxants</li> <li>• <math>\alpha</math>-agonists (pseudoephedrine)</li> <li>• <math>\beta</math>-adrenergic blockers</li> <li>• Calcium channel blockers</li> <li>• Atropine</li> </ul>	<ul style="list-style-type: none"> <li>• Alcohol consumption</li> <li>• Smoking</li> <li>• Emotional stress</li> <li>• Cold/damp weather</li> </ul>

*Most men do not experience symptoms until > 50-years-of-age; however, 80% to 90% of men > 80-years-of-age will describe voiding concerns.*

#### Key components of diagnosis

A history focuses on the lower urinary tract. A family history of prostate cancer should be noted. Medications should be reviewed (current

Table 3

## Oral therapies for BPH

Alternate medications	Selective $\alpha$ 1-blockers	5 $\alpha$ -reductase inhibitors
Phytotherapy <ul style="list-style-type: none"> <li>• Saw palmetto</li> <li>• Pumpkin seed</li> <li>• Echinacea</li> </ul> Nutraceuticals <ul style="list-style-type: none"> <li>• Coenzyme Q10</li> <li>• Lycopenes</li> </ul>	"Rapid" onset of action <ul style="list-style-type: none"> <li>• Alfuzosin</li> <li>• Doxazosin</li> <li>• Tamsulosin</li> <li>• Terazosin</li> </ul>	Large prostates respond most favourably <ul style="list-style-type: none"> <li>• Finasteride</li> <li>• Dutasteride</li> </ul>

### Quinn's case cont'd...

Quinn notes an improvement of his symptoms over the course of 1 year, but he is still not happy. Quinn's PSAs fell to 5.4 by December 2006.

He was agreeable to a trial on finasteride, but was unhappy with the results after a six-month period so he opts for transurethral resection of the prostate (TURP). Uncomplicated surgery takes place in June 2007 with 40 g resected.

After the operation, Quinn is pleased with voiding. He is taken off of urologic medications and his PSA has dropped to 2.7 at follow-up in August 2007.

and recently discontinued). Physical examination includes a rectal exam assessing:

- size,
- consistency,
- symmetry,
- tenderness and
- the presence of nodules or indurations.

Abdomen should be palpated for a suprapubic bladder mass. Bloodwork includes electrolytes and creatinine to check for renal insufficiency and a PSA test.

### Treatment options

#### Medications

The time to recommend oral therapies to a patient is when a patient's bother from his symptoms has outgrown watchful waiting and is impacting on his quality of life. Many patients want to start with an alternate medication. Add an  $\alpha$ -blocker and/or a 5 $\alpha$ -reductase inhibitor as required (Table 3). Some patients can benefit from combination therapy.<sup>3,4</sup>

There are many alternate medications. For example, saw palmetto contains  $\beta$ -sitosterol which has 5 $\alpha$ -reductase inhibitory activity. Coenzyme Q10 and lycopenes are antioxidants used to keep the balance of apoptosis to cell growth at a "younger" rate.

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**Dr. McCallum** is a Community Urologist, Capital Health Authority, Leduc, Alberta.

Long-acting selective  $\alpha$ 1-blockers relax the smooth muscle of the distal tract, but do not interfere with bladder contractility. They work quickly. They affect adrenoceptors located in the:

- prostate,
- bladder base,
- bladder neck,
- prostatic capsule and
- prostatic urethra.

5 $\alpha$ -reductase inhibitors regulate the amount of androgen available to the prostate by preventing conversion of testosterone to DHT. This slows the rate of prostatic enlargement and shrinkage of the gland can be seen. The patient must have a large gland to begin with and it can take longer to see a clinical effect.


### *Surgery*

Transurethral resection of prostate (TURP) is the most common surgery for BPH. It involves the endoscopic removal of the prostate's inner portion via the urethra. Possible complications of TURP include:

- post-operative irritative voiding,
- dry ejaculate,
- erectile dysfunction, or
- the need for a second procedure.<sup>3</sup>

### *When do you refer to a Urologist?*

Referral to a Urologist should be done:

- when satisfaction is not achieved with medication alone,
- after acute retention requiring catheterization,
- with an abnormal PSA, or
- when the patient requests. 

## Take-home message

BPH is a common condition and its prevalence is going to increase as the population ages.

Progression is associated with:

- increased prostate volume,
- symptom severity,
- risk of retention,
- need for surgery and
- a reduced quality of life.

Medical treatment is quite effective; however, surgery is the ultimate treatment.

Table 4

### Surgical treatment options

- TURP: gold standard for moderately-sized prostates
- Transurethral incision of the prostate for small obstructing glands
- High intensity focused ultrasound
- Transurethral microwave therapy
- Holmium laser enucleation of the prostate has no size limitation
- Open prostatectomy for very large prostates
- Intraprostatic stents for poor anesthetic candidates

#### References

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4. McConnell JD, Roehrborn CG, Bautista OM, et al: The Long-Term Effect of Doxazosin, Finasteride and Combination Therapy on the Clinical Progression of Benign Prostatic Hyperplasia. *N Engl J Med* 2003; 349(25):2387-98.