A 73-Year-Old Man With Symptomatic Benign Prostatic Hyperplasia

Michael J. Barry, MD, Discussant

DR PARKER: Mr B is a 73-year-old man who has had "prostate trouble" for several years. A former government employee, he lives in a suburb of Boston with his wife and daughter, and is covered by Medicare. He sees Dr N at a primary care practice at the Beth Israel Deaconess Medical Center.

On a routine physical examination in 1993, he was noted to have a "firm" large prostate with a possible right prostatic nodule. At that time, he had no urinary symptoms. A prostate-specific antigen (PSA) level was 1.4 ng/mL. By the time of his urologic evaluation in early 1994, Mr B was complaining of nocturia every hour. Six biopsy specimens of the prostate were negative for malignancy, and the results of an ultrasound of the prostate were normal. Postbiopsy prostateitis was treated with a 6-week course of ciprofloxacin. Doxazosin (1 mg at bedtime) was prescribed to help alleviate symptoms of benign prostatic hyperplasia (BPH). He did not complain of dysuria, urinary retention, or urinary incontinence.

His medical history included coronary artery disease with a coronary artery bypass graft with uneventful recovery, elevated cholesterol levels, and glaucoma. Medications included doxazosin (2 mg at bedtime), aspirin (81 mg daily), atenolol (25 mg daily), triamterene with hydrochlorothiazide (Dyazide; 1 tablet, 25 mg of hydrochlorothiazide, 37.5 mg of triamterene daily), nifedipine (30 mg XL daily), lovastatin (20 mg daily), and timolol and dipivefrin hydrochloride drops (Propine, Allergan Pharmaceuticals, Irvine, Calif) for glaucoma.

The doxazosin was increased to 4 mg at bedtime but Mr B remained very symptomatic with nocturia. His urologist then added finasteride, 5 mg per day. Mr B felt that his symptoms of prostatitis definitively improved after several months of finasteride. The urologist suggested discontinuing treatment with doxazosin because it seemed to have little impact on his symptoms.

Mr B otherwise remained in good health with normal vital signs, clear lungs, and an unremarkable cardiac, abdominal, and peripheral vascular examination. By 1995, he continued to have difficulty with urinary frequency. He reported voiding every 2 to 2½ hours during the day, but more frequently at night. Dyazide therapy was discontinued, as it possibly contributed to his urinary frequency. The doxazosin was then reinstituted, and later increased to 8 mg at bedtime. Dr N provided careful instructions regarding the risks of orthostatic hypotension. The nifedipine therapy was discontinued and his blood pressure remained under good control.

By summer 1997, Mr B complained of worsening symptoms, waking as often as 6 times per night to urinate. Though the strength of the urinary stream was "not bad," the nocturia had become unbearable. His current medications are doxazosin (8 mg at bedtime), finasteride (5 mg daily), atenolol (25 mg daily), aspirin (325 mg daily), lovastatin (80 mg daily), and timolol and Propine drops. Though he has not had any further problems from infection or any difficulties with urinary retention, renal failure, or urinary incontinence, the urinary frequency and nocturia have worsened. Both his internist and urologist are advising a surgical procedure.

MR B: HIS UNDERSTANDING AND PERCEPTIONS

Mr B: I began having trouble about 3 years ago. That's when I first started taking medication for the condition. I was finding that my urine flow wasn't as good as I thought it should be and it was dribbling. When I was taking the medicines, I seemed to be going more rather than less. Instead of getting up 3 or 4 times during the night, I was up 5 or 6 times. I needed to get some sleep and decided to talk to the doctor about it.

I'm concerned because I have several friends who have experienced the same type of surgery that the doctor recommended. They had a lot of bleeding. That didn't make the idea of surgery too appealing to me. I wouldn't mind a little blood, if it would take care of things, as I've experienced surgery many times over the years. But I was a bit reluctant. I saw the urologist, and he did the necessary work to get me on the road to surgery. But I kept putting off the surgery. I couldn't really spare the time away from things I felt I was obligated to do.

DR N: HIS UNDERSTANDING AND PERCEPTIONS

Dr N: Mr B is a remarkable gentleman who has made an amazing change in his life over the years I've known him. He has greatly improved his condition with respect to his cardiovascular disease. His major complaint now is nocturia. It's quite disruptive to him. He gets up 4 and sometimes even 6 times a night. He has had less difficulty with hesitancy and decreasing urinary stream than other patients have.

This is a common problem, but many patients don't like to deal with it or even talk about it. But when you ask them, many patients are really disrupted by prostatic symptoms and dis-
There also is the risk of prostate cancer, an important disease.

Mr B has had serious underlying cardiovascular disease, but he has been remarkably stable. He is doing well, in active, and has a very full life. I've pretty much used up the options I have medically to treat him. So my feeling would be that since we've excluded cancer previously, he might be a candidate for surgery at this time. I'd like to ask Dr Barry 3 questions: would antibiotics be of any value for minimal prostatitis seen on biopsy specimens 2 years ago? Would any other therapies help alleviate his nocturnal symptoms? Would he recommend surgery?

**AT THE CROSSROADS: QUESTIONS TO DR BARRY**

How common is BPH and symptomatic BPH unresponsive to medical therapy? What prostate symptoms can men in various age groups expect? How effective is medical therapy for BPH? What is "failed" medical therapy? What are the treatment approaches for patients such as this? When should a urologist be consulted? What is the role of surgical intervention? What procedures are currently available? What do you recommend for this patient?

**DR BARRY:** For 3 years, Mr B has had bothersome urinary tract symptoms, frequency and nocturia. His low PSA level, ultrasound, and biopsy examinations revealed no evidence of prostate cancer, but histologic evidence of prostatitis. Symptoms did not consistently improve with antibiotics, and Mr B has been treated medically with a combination of an α-blocker and a 5α-reductase inhibitor at full doses since 1995. With time, his symptoms may actually have worsened on this combination, and he is now considering surgery.

**Diagnosis**

For men in Mr B's age group with lower urinary tract symptoms, the most likely diagnosis is BPH. Benign prostatic hyperplasia may affect as many as 40% of men in their 70s. Other considerations include urethral stricture disease or primary diseases of the bladder, particularly a hypotonic or uninhibited bladder without bladder outlet obstruction. Genitourinary infections or cancers also need to be considered. The absence of a history of urologic instrumentation or venereal disease makes a stricture less likely, and the absence of a history of diabetes or a neurologic disorder makes primary bladder pathology less likely. Given Mr B's case presentation, infection or cancer as a primary cause of these symptoms is unlikely. Nevertheless, a substantial minority of men with a clinical diagnosis of symptomatic BPH cannot be demonstrated to have bladder outlet obstruction on formal urodynamics studies, that is, on simultaneous measurements of bladder pressure and urinary flow.

The traditional view of the mechanism by which the histologic process of BPH leads to lower urinary tract symptoms has been that the expanding prostatic adenoma results in bladder outlet obstruction, often with secondary changes in the bladder. However, several empirical observations cast doubt on this process as the sole mechanism, including the poor correlation of urodynamic measurements with symptom severity, the improvement in symptoms with treatment that correlates poorly with reductions in the degree of outlet obstruction, and that men who are not urodynamically obstructed respond almost as well to prostatectomy as obstructed men.

As a result of this uncertainty, 2 schools of thought coexist regarding diagnosis. One is that a few minimal tests—a digital rectal examination, focused neurologic examination, urinalysis, serum creatinine, and perhaps a serum PSA level—are adequate to establish a clinical diagnosis in the right epidemiologic context. The other is that outflow obstruction should be documented urodynamically, particularly before men are subjected to surgical therapy. Unfortunately, insufficient data are available to determine whether formal urodynamics, which are somewhat invasive and expensive, improve patient outcomes. Some physicians prefer an intermediate diagnostic approach of noninvasively measuring a urinary flow rate. A low flow rate of less than 10 to 15 mL/s with an adequate voided volume makes outflow obstruction more likely. Some men, however, will have low flow in the absence of outflow obstruction because of a flaccid bladder, while others with outflow obstruction will maintain their flow rate with a vigorous bladder contraction.

What about Mr B's case? Some physicians would worry his dominant symptoms of frequency and nocturia represent a "red flag" suggesting an alternate diagnosis, as men with symptomatic BPH generally have both bladder filling (urgency, frequency, and nocturia) and voiding (weak stream, hesitancy, intermittency, and incomplete emptying) symptoms. Although the latter symptoms are not highlighted in Mr B's case presentation, it is not clear whether he does not have these symptoms or whether he is simply not as bothered by them. It would be helpful at this point to obtain Mr B's answers to the American Urological Association (AUA) Symptom Index (Figure), a reliable and valid instrument to measure the severity of lower urinary tract symptoms associated with BPH. This 7-item self-administered questionnaire, which takes only a few minutes to complete, is widely used by urologists, more objectively quantifies a patient's symptom burden, and more reproducibly measures changes in symptoms over time and with treatment.

1. Over the past month or so, how often have you had a sensation of not emptying your bladder completely after you finished urinating?
2. Over the past month or so, how often have you had to urinate again less than 2 hours after you finished urinating?
3. Over the past month or so, how often have you found you stopped and started again several times when you urinated?
4. Over the past month or so, how often have you found it difficult to postpone urination?
5. Over the past month or so, how often have you had a weak urinary stream?
6. Over the past month or so, how often have you had to push or strain to begin urination?
7. Over the last month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?

**AUA Symptom Score = Sum of Questions 1–7**

Adapted from the American Urological Association (AUA) Symptom Index for benign prostatic hyperplasia (range, 0–35 points), reproduced with permission from Barry et al. For the last 6 questions, after the possible answers (score for each answer is in parentheses): not at all (0); less than 1 time in 5 (1); less than half the time (2); about half the time (3); more than half the time (4); almost always (5). Question 7 is answered using the following possibilities: none (0); 1 time (1); 2 times (2); 3 times (3); 4 times (4); 5 or more times (5). Total the points for the AUA symptom score.
Given Mr B's symptoms, which appear to be predominantly filling symptoms and a failure of response to medical therapy, it would be reasonable to measure his urinary flow rate. If the flow rate were unexpectedly high, one could consider a pressure-flow study to confirm the diagnosis. The evidence supporting this diagnostic approach, however, is weak.

Physicians should remember to look for nonurologic factors that may exacerbate lower urinary tract symptoms. The patient should not be using medications that can impair bladder contractility or increase outlet obstruction, including over-the-counter allergy and cold preparations. Consumption of fluids in the evening, particularly caffeinated beverages, can certainly exacerbate nocturia. With Mr B's history of heart disease, one would also want to be sure that the nocturnal diuresis that can be seen with congestive heart failure is not a factor, particularly with prominent nocturia. He was taking diuretics in the past and is not taking them currently. One can easily exclude diabetes as a cause of these symptoms.

Finally, it is important to look for prostate cancer among men with symptoms suggesting BPH. Although early prostate cancer is generally asymptomatic, symptomatic BPH and prostate cancer can coexist. Prostate cancer is found in 10% to 15% of men undergoing prostatectomy for BPH. Interestingly, screening studies have not shown that lower urinary tract symptoms raise the probability of finding prostate cancer. Seeking evidence of prostate cancer in men with symptomatic BPH must therefore be considered screening. The major debate is whether men with lower urinary tract symptoms and a digital rectal examination not suspicious for prostate cancer should have a PSA test to reduce the probability of a coincidental prostate cancer. Such testing should be considered optional, as mildly elevated PSA values are common in both men with BPH and localized prostate cancer, and because of the uncertainty whether early detection of prostate cancer improves outcomes. Two studies have now shown a poor negative predictive value of PSA in the setting of BPH. In a study of a recent National Institutes of Health trial in which a large group of men with BPH underwent biopsies, the mean PSA levels among men found to have prostate cancer vs men with only BPH were 3.5 and 3.0 ng/mL, respectively—not a great degree of discrimination. Moreover, even advocates of early detection doubt its value in men with less than a 10-year life expectancy, or after about the age of 74 years for men with average comorbidity.

What are clinicians and patients like Mr B to do about PSA testing in the setting of lower urinary tract symptoms given this controversy? Clinicians should discuss with their patients the possibility of an underlying prostate cancer, the ways one might look for it, and the uncertainty about whether finding it would make any difference, particularly in light of their age and health. Several recent reviews have addressed the topic of early detection of prostate cancer in detail.

Natural History of BPH

The natural history of men with BPH depends on their symptom levels at baseline. In 1 study of men with a diagnosis of BPH who elected "watchful waiting" despite being reasonable candidates for surgery, men with mild symptoms were relatively unlikely to progress to severe symptoms or require surgery, while men with severe symptoms at baseline often continued to be severely symptomatic or opt for treatment over time. Among these men, the risk of acute urinary retention was about 2.5% per year.

Medical Therapies for BPH

For men like Mr B who have symptomatic BPH, the purpose of treatment is to reduce or relieve bothersome urinary symptoms and to reduce the risks of complications, including acute urinary retention and obstructive uropathy. Most men who tire of simple "watchful waiting" will be treated with some form of medical therapy. Two basic approaches are available for medical management, 5a-reductase inhibition (finasteride) and a-adrenergic blockade (prazosin, terazosin, doxazosin, and tamsulosin). The traditional view is that 2 components contribute to prostatic obstruction: a static component related to pure mechanical obstruction and a dynamic component related to a-adrenergic tone in the prostate, prostatic capsule, and bladder neck. The 5a-reductase inhibitor finasteride presumably targets the static component, and a-blockers, the dynamic component. Mr B has taken both.

Finasteride blocks the conversion of testosterone to diltroxytestosterone, the major intraprostatic androgen. With finasteride treatment over 6 to 12 months, reductions in prostate volume averaging about 20% have been observed. Symptoms can improve, although clinical trials have suggested that the average symptom improvement is quite modest, and its clinical significance can be questioned. In a Veterans Affairs (VA) study comparing the 1-year outcomes of treatment with finasteride vs the a-blocker terazosin, finasteride was no more effective than placebo at reducing symptoms. However, this trial has been criticized for enrolling men with large prostates. A subsequent meta-analysis of 7 finasteride trials documents that the improvement in symptoms with finasteride relative to placebo depends on prostate volume, with average symptom responses being best (though still quite modest) among men with prostate glands greater than 40 g.

Interestingly, despite the relatively small average impact on symptoms, recent research suggests that finasteride has a major impact on reducing the rate of acute urinary retention and of progression to surgical treatment. A meta-analysis of finasteride studies has documented a relative reduction in acute retention of 57% (95% confidence interval [CI], 38%–72%) and of progression to surgery of 24% (95% CI, 15%–49%). As the absolute rates of these events remain low, about 40 men would have to be treated with finasteride for 2 years to prevent 1 event of acute retention or surgery.

Mr B apparently has not experienced adverse effects from his treatment with finasteride. Indeed, the adverse effects of finasteride are relatively minor, consisting primarily of sexual dysfunction in about 5% of men. Because finasteride lowers PSA levels about 50%, these levels need to be interpreted differently among men taking finasteride, but there is no empirical evidence that finasteride interferes with the detection of prostate cancer. Finasteride does not require dose titration; the dose is 5 mg daily. However, men may require a prolonged trial for as long as 6 months to a year before one can conclude the drug has been ineffective.

a-Adrenergic receptor blockers have been used for the treatment of BPH for decades. Selective a-blockers such as prazosin, terazosin, doxazosin, and tamsulosin have similar efficacy and fewer adverse effects than older, nonselective a-blockers. Clinical trials have consistently found that these agents reduce lower urinary tract symptoms in the setting of a clinical diagnosis of BPH. For example, in the VA trial discussed earlier, mean AUA scores dropped from about 16 to 10
points with terazosin (compared with 16 to 14 points with placebo), and 61% of men reported they were moderately or markedly improved after 1 year of treatment with terazosin (compared with 38% for placebo). One randomized trial showed treatment with the α-blocker alfuzosin also significantly decreased the occurrence of acute urinary retention. In general, the available α-blockers appear to show similar efficacy, although head-to-head comparisons are lacking.

The adverse effects of α-blockers include dizziness, asthenia, and postural hypotension. α-Blockers do not appear to affect PSA levels. Doses of α-blockers need to be titrated upward to find the dose that relieves symptoms satisfactorily while minimizing any adverse effects. Underdosing with α-blockers is often a major reason for lack of effectiveness. Two to 4 weeks at a given dose level are usually long enough to assess the therapeutic response.

α-Blockers are the preferred agents for reducing lower urinary tract symptoms in men with a clinical diagnosis of BPH, regardless of prostate size. The ability to reduce rates of BPH complications, however, is more firmly established for finasteride. While data from the VA trial suggested that the combination of finasteride and terazosin was not better at relieving symptoms than terazosin alone, the strategy of combining these 2 agents, particularly in men with larger prostates, while untested, is conceptually attractive and was the strategy pursued for Mr B. He has been treated with the combination of finasteride and doxazosin for about 2 years, and his doxazosin dose has been pushed up appropriately to the maximum recommended level.

Men do not need an accurate ultrasonographic measurement of prostate size for decision making about drug therapy for BPH. Digital rectal examinations often underestimate prostate size, when correlated with ultrasonographic measurements. Recent data have also suggested that PSA levels may serve as a proxy for prostate size in terms of predicting symptomatic response to drug therapy with finasteride.

Two other medical treatments are available for BPH, phytotherapy and antibiotic treatment for prostatitis. Phytotherapy, or treatment with plants and plant extracts, has been widely used for BPH in Europe. Evidence that these therapies are efficacious is inconclusive because of the lack of properly designed trials. I doubt that phytotherapy would be helpful for Mr B. Recently, histologic evidence of prostatitis has been commonly found when men undergo biopsies for an elevated PSA level, and prostatitis may coexist with BPH. Prostatitis is found more often in men with larger prostates. Men with these findings may receive a course of antibiotics for prostatitis, although the great majority of cases of chronic prostatitis are probably not bacterial in origin. Further research is needed on the relationship between BPH and prostatitis, and particularly on the therapeutic implications of this dual diagnosis. However, since Mr B had already undergone a course of antibiotics after his previous biopsy, another course would be unlikely to help.

Despite treatment with a combination of finasteride and doxazosin, Mr B is nevertheless dissatisfied with his situation. Therefore, he has failed medical therapy. There are few data on the long-term cumulative incidence of failure of medical therapy, particularly outside the artificial environment of clinical trials.

Surgical Therapies for BPH

Surgical therapies for BPH include prostatectomy, the traditional option considered by many to be the "gold standard" for symptom reduction and prevention of BPH complications, and a number of new less invasive procedures.

Prostatectomies are usually done transurethrally, unless the prostate is exceedingly large, in which case the older open prostatectomy may be performed. A transurethral resection of the prostate (TURP) is very effective at relieving lower urinary tract symptoms in men with a clinical diagnosis of BPH, and much more effective, on average, than the pharmacologic therapies. For example, in 1 study, mean AUA scores fell from 18 to 7 points just 1 month after surgery. In another, 85% of patients rated themselves markedly improved after TURP. Men whose symptoms are extremely bothersome are especially likely to benefit. TURP also substantially reduces the risk of complications from BPH.

TURP is usually performed with spinal anesthesia, and even men with stable cardiac disease like Mr B can undergo the procedure with no special cardiac evaluation. A catheter is usually required for a few days. Lengths of hospital stay have fallen with TURP, with some recent reports of discharges after an overnight stay. In 1 study, 81% of men did not report any additional bed-days after returning home, and 61% were out and about within a week of discharge.

Thirty-day mortality following TURP has fallen steadily over time and was about 0.8% for Medicare-age men in 1990. An early report of increased delayed long-term mortality following TURP compared with open prostatectomy has been contradicted by subsequent studies. Greater comorbidity among men subjected to TURP may explain this earlier finding, but studies to substantiate that hypothesis have conflicted.

In general, TURP is a durable treatment—about 5% of Medicare-age men underwent reoperation for BPH over 7 years. Despite the traditional view that sexual dysfunction and incontinence were complications of the procedure, a VA trial that randomized men to immediate transurethral resection vs a strategy of "watchful waiting" did not document a higher risk of either sexual dysfunction or incontinence with TURP. Retrograde ejaculation, however, is commonly experienced. TURP also has short-term risks, including bleeding, which Mr B was very concerned about, and medical complications such as urinary tract infections or thromboembolism. In the VA trial, only 1% of surgical patients required transfusions, while another 1% had medical complications. Bladder neck contractures or urethral strictures following prostatectomy requiring either dilation or endoscopic surgery occurred in about 6% of men over 3 years.

Although the complication rate of prostatectomy is relatively low, great interest exists in developing less invasive approaches to the treatment of BPH with fewer adverse effects than TURP, yet greater effectiveness than medical therapy. Surgical approaches include transurethral incision of the prostate (TUIP), laser therapy, and electrical vaporization.

TUIP involves incising the prostate without resecting tissue and appears about as effective initially as TURP among men with smaller prostates. TUIP appears to have a smaller risk of bleeding, retrograde ejaculation, and urethral stricture than TURP, but, without tissue resection, the long-term durability of the procedure has been a concern. Laser energy can be used to coagulate or actually vaporize prostate tissue.

Free-beam and contact lasers are used to apply this energy from outside the prostate, while interstitial lasers are used to coagulate tissue from within the prostate, sparing the urothelium. High-power laser vaporization can be thought of as
Simply performing a TURP with a laser energy source rather than an electrical resection loop. The free-beam or contact techniques using lower power levels coagulate tissue that subsequently sloughs, while the interstitial technique generally does not create a tissue defect. In the short term, laser operations appear to cause less bleeding and, as a result, may often be done as same-day surgery. However, the coagulation techniques in particular can be associated with persistent, irritative lower urinary tract symptoms and the need for prolonged catheterization. The plethora of techniques makes evaluation of the therapeutic effect of lasers relative to standard TURP difficult. In general, short-term symptom relief (after the resolution of any irritative symptoms related to the procedure) has been comparable or slightly favor TURP. Whether long-term symptom relief will be as good requires longer follow-up.

Electrical vaporization involves a rotating electrode or high current settings to vaporize superficial prostate tissue while coagulating deeper levels. Bleeding appears to be less of a problem than with TURP, which may be of interest to Mr B. Shorter catheterization times and hospital stays are counted as an advantage by advocates. However, postoperative irritative symptoms can be problematic. Case series with short-term follow-up suggest reductions in symptoms approaching the magnitude seen with TURP, but good comparative trials are not available, and long-term outcomes are undefined. Costs are shown in the Table.

**Device Therapies for BPH**

Device therapies for BPH include transurethral microwave thermotherapy (TUMT) and transurethral needle ablation (TUNA). TUMT involves using a urethral device to generate microwaves to heat and coagulate prostate tissue while simultaneously cooling the urethra to protect it from injury. As prosthetic pain originates largely from the urethra, the procedure can generally be performed without regional or general anesthesia. TUMT, which can be done in a single sitting, does not result in tissue sloughing. The optimal energy settings are under active investigation. Higher-energy settings may be more effective, but may also require more anesthesia. The mechanism of its effect on symptoms is not entirely clear and may involve damage to sensory nerves as well as some relief of bladder outlet obstruction. Randomized trials against sham procedures or TURP suggest the procedure is effective at relieving symptoms, but less so than TURP. Follow-up over several years has suggested a relatively high cumulative incidence of needing additional therapy, at least with lower-energy settings. Complications can include short-term irritative symptoms, hematuria (seldom requiring transfusion), and the need for prolonged catheterization due to urinary retention, which has been relatively high in some studies. Sexual dysfunction, including retrograde ejaculation, appears to be rare.

TUNA is another device therapy that involves heating and coagulating prostate tissue using radiofrequency energy delivered via a needle placed transurethrally into the prostate. A proximal sheath on the needle protects the urethra. Tissue sloughing or cavities are not created, and again the mechanism of effect is unclear. Depending on the size of the prostate, 1 or 3 areas are coagulated in each lobe. Like TUMT, short-term hematuria, irritative symptoms, or urinary retention may result, with apparently few long-term complications. Although case series suggest a good short-term impact on symptoms, clinical trials comparing TUNA with sham treatment or TURP are not available, and long-term outcomes of the procedure are undefined.

**Conclusion**

What would be the optimal approach for the treatment of Mr B? Provided the diagnosis is confirmed, TURP would likely have a substantial favorable impact on his symptoms, with the expectation of durable benefits for many years, and a much lower risk of complications following the natural history of BPH. However, he might choose a laser or electrical vaporization approach to reduce short-term problems with bleeding, although the bleeding with TURP is certainly manageable. Whether he would sacrifice any long-term effectiveness with these procedures is not well documented. Alternatively, he might elect TUMT or TUNA, probably the easiest treatments to undergo, although potentially with the need for catheterization over the short run. Mr B might expect less impact on his symptoms than with TURP, however, and he would need to accept the fact that the long-term effectiveness of these treatments is undefined. Moreover, insurance coverage for TUMT and TUNA can be problematic. For example, Medicare coverage for these procedures varies state by state; in Massachusetts, neither is routinely covered.

As with so many areas of medicine, how primary care clinicians and specialists, in this case, urologists, should share care to get the best possible outcomes for patients like Mr B has been poorly studied. The basic diagnostic evaluation and the initiation and monitoring of medical therapy can be performed in primary care, and there are many excellent references to help in this regard. However, when the diagnosis is unclear and urodynamic evaluation is necessary, the response to initial medical management has been unsatisfactory, or the patient wishes a detailed discussion of invasive treatment, urologic consultation can be exceedingly helpful.

For Mr B, there are many more choices for the treatment of his symptoms than there were just 5 years ago. Unfortunately, at present there are few good randomized comparisons of different strategies of treatment to help guide him in his choice. In the meantime, the right decision for Mr B depends on his feelings about the trade-off between a greater potential for long-term symptom relief with more invasive treatment, and a po-
tentially loss satisfactory outcome with less invasive treatment. He is the best person to weigh those trade-offs. I wish him luck!

QUESTIONS AND DISCUSSION

[EDITOR'S NOTE: Mr B was unable to attend the conference due to illness in the family.]

AN INTERNIST: Evidence now suggests that for the sexually inactive man, LH-RH [luteinizing hormone-releasing hormone] agonists may be very useful for medically treating patients with BPH. Also, a critical issue facing the primary care internist or the surgeon is a patient with BPH symptoms that has a PSA between 4 and 10 ng/mL. What should clinicians do about men with symptomatic BPH with mildly elevated PSA levels, and how far should one go to rule out cancer? Should one biopsy, and if the initial biopsy is negative should one rebiopsy? Is it useful to look at free vs bound PSA?

DR BARRY: In the absence of outcomes data clinicians reasonably can take different approaches. Most clinicians will biopsy once, the first time, for an elevated PSA in the 4 to 10 ng/mL range, if the patient is a candidate for aggressive treatment with radiation therapy or radical prostatectomy. Others would argue for making biopsy decisions based on age-specific reference ranges. For example, for men in their 70s, the age-specific reference range for PSA is up to 6.5 ng/mL, and some would not biopsy unless the PSA were higher than that. Others who don't want to trade any specificity for sensitivity would biopsy patients with PSA levels as low as 2.5 ng/mL, and might rebiopsy even if the first set of biopsies was negative. The ratio of free PSA to total PSA, which tends to be lower in men with prostate cancer than BPH, is being proposed by some experts as a technique to reduce the number of biopsies for men with PSA levels in the 2.5 to 10 ng/mL range. The number of biopsies one will avoid by weeding out men with relatively high ratios of free to total PSA is actually relatively small, only about 20%. On your former point, LH-RH agonists, or medical androgen deprivation, are only somewhat more effective than finasteride at reducing prostate size, and symptom reduction has still only been modest. For many men the side effects of androgen deprivation would be unacceptable, but it may be an option for a small number of men.

DR DELBANO: What has been the impact of more formally giving patients choices? Do they tend to have more or less surgery compared with control groups?

DR BARRY: For BPH, the results of clinical trials of formal decision support systems have conflicted. In some studies, substantial reductions in the rates of TURP have occurred. Other studies, particularly in managed care organizations that already have very low rates of surgery, have not demonstrated much impact. The national trend is toward less surgery. The number of prostatectomies done in the United States annually has decreased from about 400,000 in 1987 to about 200,000 now. This trend is related to better medical treatments and the additional surgical options now available, as well as greater patient involvement in decision making.

AN INTERNIST: α-Blockers are fairly potent in terms of their side effects of orthostatic hypotension. Could you comment on dosing for the α-blockers in terms of how much more efficacy you get at escalating doses of medicine?

DR BARRY: This is one area where my own sense from clinical practice differs somewhat from what is reported in the trials. Clinical trials of α-blockers show relatively small proportions of men stopping therapy because of side effects, at least over 6 months to a year. As we generally treat a broader spectrum of men with more medical problems in clinical practice, it's not surprising that more intolerance occurs. The problem is that the dose response to α-blockers has been relatively steep. So higher doses generally give a better therapeutic response, but often more side effects. A current area of interest is the development of "uro-selective" α-blockers that specifically block prostatic α-adrenergic and not the α-adrenergic receptors in vascular smooth muscle. Tamsulosin, which is just becoming available in the United States, is designed to be one of these agents. The clinical data, however, are not yet convincing, at least to me, that pharmacologic uroselectivity will actually reduce side effects relative to therapeutic efficacy. The bottom line is that pushing up the dose of an α-blocker as high as people will tolerate is reasonable to get maximal effectiveness, but in clinical practice not everyone will tolerate that strategy. In my judgment, another common reason that α-blockers are stopped is that symptoms like dizziness and weakness also happen frequently for many other reasons. If we always attribute them to the α-blocker when they occur and stop, we may not keep any patient on therapy for any length of time. So the concept of rechallenge with the α-blocker, particularly for minor side effects that have prompted stopping the drug, may be a good strategy in primary care for trying to be sure patients like Mr B have an adequate trial of medical therapy.

Dr Barry's work is supported by grant HS8697 from the Agency for Health Care Policy and Research.

Clinical Crossroads is made possible by a grant from the Robert Wood Johnson Foundation. We thank the patient and his doctor for sharing their stories in person and in print.

References
48. Catalona WJ, Smith DS, Ormsen DK. Prostate cancer detection in men with serum PSA concentrations of 2.6 to 4.0 ng/mL and benign prostate examination. JAMA. 1997;277:1428-1436.