INTRODUCTION — Benign prostatic hyperplasia (BPH) becomes increasingly common as men age (figure 1). BPH can lead to urinary symptoms that may benefit from medical or surgical treatment. However, many men with BPH are asymptomatic or have only mild symptoms and may not require therapy.

The medical therapy of BPH will be reviewed here. Surgical and other invasive therapies, the clinical manifestations, natural history, diagnosis of BPH, and the epidemiology and pathogenesis of BPH are all discussed separately. (See “Surgical and other invasive therapies of benign prostatic hyperplasia” and “Clinical manifestations and diagnostic evaluation of benign prostatic hyperplasia” and “Epidemiology and pathogenesis of benign prostatic hyperplasia”.)

Lower urinary tract symptoms (LUTS) in men of uncertain etiology, or from etiologies other than BPH, also are discussed separately. (See “Lower urinary tract symptoms in men”.)

DEFINITIONS — A number of different terms and abbreviations are used when discussing symptomatic BPH. These include:

- Lower urinary tract symptoms (LUTS)
- Benign prostatic enlargement (BPE)
- Benign prostatic obstruction (BPO)
- Bladder outlet obstruction (BOO)

BPE is the physical enlargement of the prostate that occurs as the result of the histologic changes of BPH. BPO is BOO in the setting of BPE.

BPE and BOO secondary to BPH are frequently diagnosed clinically on the basis of LUTS. We will use the abbreviation BPH/LUTS for LUTS presumed to be secondary to BPH, sometimes called symptomatic BPH.

INDICATIONS FOR THERAPY — The common symptoms of BPH are increased frequency of urination, nocturia, hesitancy, urgency, and weak urinary stream. These symptoms typically appear slowly and progress gradually over a period of years. (See “Clinical manifestations and diagnostic evaluation of benign prostatic hyperplasia”, section on ‘Natural history’.)

In general, these symptoms only require therapy if they have a significant impact on a patient’s quality of life [1]. Even without therapy, many men will experience stabilization or improvement in symptoms over time [2]. One review found that over a follow-up period of 2.6 to 5 years, 16 percent of men had stable symptoms and 38 percent improved [3]. Thus, the decision to treat BPH/LUTS involves balancing the severity of the patient’s symptoms with potential side effects of therapy.

BPH may also require therapy if BOO is creating a risk for upper tract injury such as hydronephrosis or renal insufficiency, or lower tract injury such as urinary retention, recurrent infection, or bladder decompensation (eg, low pressure detrusor contractions; post-void residuals of >25 percent of total bladder volume) [4]. In general, patients who develop these symptoms will require invasive therapy [2]. (See “Surgical and other invasive therapies of benign prostatic hyperplasia”.)

The decision to treat is usually based on the severity of symptoms and the patient’s tolerance for these symptoms. Use of the AUA symptom score (also known as the International Prostate Symptom Score [IPSS]) (table 1) permits quantitation of symptom severity and monitoring of symptom progression over time. Additionally, the IPSS adds a question about “bother” to the AUA score. These questionnaires are easy and quick to complete; however, not all clinicians use them to assess symptoms.

Urine flow rate during voiding can also be easily measured. This is a noninvasive test that is readily available to urologists, but usually is not available to primary care clinicians. Thus, medical treatment usually is initiated on the basis of symptoms in the primary care setting.

When symptoms occur in the setting of autonomic or severe peripheral neuropathy or following invasive treatment of the urethra or prostate, patients should be referred for urologic evaluation rather than started on treatment by a primary care clinician.

AGENTS — The bladder outlet obstruction of BPH has two components:

- A dynamic (physiologic, reversible) component related to the tension of prostatic smooth muscle in the prostate, prostate capsule, and bladder neck
A fixed (structural) component related to the bulk of the enlarged prostate impinging upon the urethra

Two classes of drugs, alpha-adrenergic antagonists and 5-alpha-reductase inhibitors, act upon the dynamic and fixed components of bladder outlet obstruction, respectively.

Alpha-adrenergic antagonists appear to be more effective than 5-alpha-reductase inhibitors for short-term and long-term treatment of BPH/LUTS [5]. However, only 5-alpha-reductase inhibitors have demonstrated the potential for long-term reduction in prostate volume and need for prostate surgery. The use of agents from both classes in combination may be superior to using either class alone.

Antiandrogens and gonadotropin-releasing hormone (GnRH) agonists also have been used. GnRH agonists may be somewhat more effective for BPH/LUTS than the above medications, but the resulting androgen deficiency generally makes their use unacceptable to patients.

Studies, using surveys and claims data, have examined which therapies are most commonly chosen for patients [6-8]. In the United States, many patients are initially managed with watchful waiting [6]; those who are prescribed a medication are most likely prescribed an alpha-adrenergic antagonist [6,8]. Initial management with watchful waiting appears to be somewhat less common in Europe; initial therapy with an alpha-adrenergic antagonist appears to be most common [7].

**Alpha-1-adrenergic antagonists** — Five long-acting alpha-1-antagonists, terazosin, doxazosin, tamsulosin, alfuzosin, and silodosin have been approved by the Food and Drug Administration in the United States for treatment of the symptoms of BPH [9]. Prazosin, a short-acting alpha-1-antagonist, is generally not used for BPH, due to need for frequent dosing and the potential for more cardiovascular side effects.

**Mechanism** — Alpha-1-adrenergic antagonists such as terazosin act against the dynamic component of bladder outlet obstruction by relaxing smooth muscle in the bladder neck, prostate capsule, and prostatic urethra.

Alpha-1 receptors are abundant in the prostate and base of the bladder, and sparse in the body of the bladder [10,11]. The density of these receptors is increased in hyperplastic prostatic tissue [12].

Three alpha-1 adrenoreceptor sub-types have been characterized: 1A, 1B, and 1D. Terazosin, doxazosin, and alfuzosin antagonize all three receptor subtypes with similar affinity, whereas tamsulosin demonstrates relative selectivity for alpha-1A and -1D receptors [13]. Silodosin is a relatively selective alpha-1A receptor antagonist [14].

Alpha-1A subtype receptors comprise approximately 70 percent of adrenoreceptors in prostate tissue whereas alpha-1B receptors are more prevalent in smooth muscle of the vasculature [15,16]. The alpha-1D subtype receptors comprise less than 30 percent of prostatic adrenoreceptors and are located in prostatic stromal elements [16]. Alpha-1D receptors are also found in the detrusor muscle of the bladder, bladder neck, and the sacral region of the spinal cord [16].

In one report, there was a direct relationship between the smooth muscle content of prostatic tissue and the increase in maximal urinary flow rate in men with BPH treated with terazosin [17]. In vitro studies showed that terazosin and doxazosin, but not tamsulosin, caused prostatic apoptosis [18,19]. In a randomized trial of over 500 men with LUTS treated for three months with alfuzosin, there was no reduction in prostate volume [20]. Changes in prostate volume have not been shown to correlate with clinical efficacy.

**Efficacy** — The approved alpha-1-adrenergic antagonists appear to have similar efficacy [21-22], although there have been few direct comparisons. A meta-analysis of trials with alfuzosin, terazosin, doxazosin, or tamsulosin published prior to October 1998 provides an overview of the efficacy and side effects of these drugs [23]. There were 6333 men in placebo-controlled trials and 507 men in comparative studies. The results indicated that the drugs were more effective than placebo and that the efficacy of the drugs was similar. In the drug-treated men, the symptom scores (table 1) decreased 30 to 40 percent, and urinary flow rates increased 16 to 25 percent.

The selective alpha-1D antagonist, naftopidil, may also be effective although long term randomized controlled trials are needed prior to recommendation for use [24].

In a meta-analysis comparing alpha-adrenergic antagonist monotherapy versus finasteride (a 5-alpha-reductase inhibitor), doxazosin and terazosin were more effective in improving urinary symptoms compared to finasteride [5]. Tamsulosin and finasteride were equally effective. Alfuzosin, silodosin, and naftopidil were not studied in this meta-analysis. (See '5-alpha-reductase inhibitors' below.)

**Dosing** — Initiation and dose titration is shown in a table (table 2).

Medication therapy for BPH/LUTS is generally ongoing. Patients who remain symptomatic on a submaximal dose of an alpha-adrenergic antagonist, and are not experiencing adverse effects, should have the dose increased.

**Side effects and interactions** — In the above meta-analysis, the drugs differed in their side-effect profiles [23]. In clinical trials, the rates of withdrawal for side effects were similar to placebo for alfuzosin and tamsulosin (4 to 10 percent), while with terazosin and doxazosin an additional 4 to 10 percent of men withdrew for side effects.

The most important side effects were orthostatic hypotension and dizziness. Terazosin and doxazosin generally need to be initiated at bedtime (to reduce postural lightheadedness soon after starting the medication) and the dose should be titrated up over several weeks. If there is a hiatus in drug administration, retitration is usually required.

The hypotensive action can be useful in older men who have hypertension, but they require careful monitoring. Alpha-1-adrenergic
Medical treatment of benign prostatic hyperplasia

Antagonists may increase the incidence of heart failure when used as monotherapy for hypertension. (See "Choice of therapy in primary (essential) hypertension: Recommendations", section on 'Alpha blockers'.)

Tamsulosin, alfuzosin, and silodosin have lower potential to cause hypotension and syncope than either terazosin or doxazosin [15, 25-27], and tamsulosin may further have slighter less effect on blood pressure than alfuzosin [23]. These differential effects on blood pressure by different alpha-1-antagonists may be due to their differential blocking of alpha-1A receptor subtype [28]. (See 'Mechanism' above.)

The hypotensive effects of terazosin and doxazosin can be potentiated by concomitant use of the phosphodiesterase-5 (PDE-5) inhibitors sildenafil or vardenafil. The risks with tadalafil are less clear. We feel that men who are on lower doses of terazosin or doxazosin and are not experiencing orthostatic blood pressure changes can be treated with PDE-5 inhibitors as long as dosing is separated by at least four hours. Tamsulosin at a dose of 0.4 mg/day does not appear to significantly potentiate the hypotensive effects of sildenafil [29].

Other common side effects of alpha-1-antagonists include asthenia and nasal congestion. Tamsulosin and silodosin, in particular, can affect ejaculation. In one study, tamsulosin decreased mean ejaculate volume in more than 90 percent of patients, with 35 percent having no ejaculate; this problem was not observed with alfuzosin 10 mg [30]. Silodosin produces retrograde ejaculation in approximately 28 percent of patients [27].

5-alpha-reductase inhibitors — There are two 5-alpha-reductase inhibitors approved in the United States, finasteride and dutasteride.

Mechanism — These drugs act by reducing the size of the prostate gland. Treatment for 6 to 12 months is generally needed before prostate size is sufficiently reduced to improve symptoms. The type 2 form of 5-alpha-reductase catalyzes the conversion of testosterone to dihydrotestosterone in the prostate, hair follicles, and other androgen-sensitive tissues. Its clinical importance is suggested by the observation that men with inactivating mutations of the gene for the enzyme have very small prostate glands and do not develop BPH [31]. The type 1 form of the enzyme is present in liver, non-genital skin, and some areas of the brain [32].

Efficacy — In a multicenter trial 895 men with BPH were treated with placebo or 1 or 5 mg/day of finasteride for 12 months [33]. The following benefits were noted in the men treated with finasteride:

- Serum dihydrotestosterone concentrations decreased by about 70 percent and serum testosterone concentrations increased by 10 percent in both finasteride treatment groups.
- A reduction in obstructive and non-obstructive symptom scores by 23 and 18 percent, respectively, in the men given 5 mg daily but less in the men given 1 mg daily and none in the men given placebo.
- An increase in maximal urinary flow rate of 1.6 mL/sec in the men given 5 mg/day versus 1.4 mL/sec with 1 mg/day, and 0.2 mL/sec with placebo. The baseline value was approximately 7.3 mL/sec; values above 15 mL/sec are usually associated with no obstructive symptoms.
- A reduction in mean prostate volume by 19 and 18 percent in the two treatment groups versus 3 percent in the placebo group.

The efficacy of finasteride appears to persist with long-term treatment. As an example, a trial of over 3000 men who were treated daily with 5 mg of finasteride or placebo demonstrated that the improvements in symptom scores, maximal urinary flow rates, and prostate volume were maintained for more than four years [34]. The most important findings were that finasteride treatment decreased the probability of surgery (5 versus 10 percent, risk reduction 55 percent) and acute urinary retention (3 versus 7 percent, risk reduction 57 percent) (figure 2). Patients who remained on finasteride for six years in an open-label extension of the study had sustained benefits [35].

The efficacy of finasteride is greater in men with larger prostate volumes than in men with smaller prostate volumes. (See 'Short-term efficacy' below.)

Finasteride increases the apoptotic index of epithelial and stromal cells [36] and decreases the volume of epithelium [37]. After 12 months of treatment finasteride also decreases detrusor pressure at maximum flow rates in men with larger prostate glands (>40 mL) [38].

Finasteride also may suppress gross hematuria in those in whom other causes (particularly prostate and bladder cancer) have been ruled out [39, 40]. In a randomized trial, 57 men with BPH, evidence of bleeding from friable prostatic tissue on flexible cystoscopy, and chronic intermittent gross hematuria with no other identifiable cause were assigned to finasteride or a control arm [39]. Finasteride was associated with a lower rate of recurrent hematuria (14 versus 63 percent) and of surgery for bleeding (0 versus 26 percent).

Dutasteride is an inhibitor of both 5-alpha reductase enzymes and may be more potent than finasteride. In a trial in 4325 men with BPH, dutasteride reduced the risk of acute urinary retention by 57 percent and surgical intervention by 48 percent, and also reduced prostate volume and symptoms after 24-month follow-up [41]. A subsequent trial found similar results after 48-month follow-up in men with BPH randomly assigned to dutasteride, compared to placebo [42].

The Enlarged Prostate International Comparator Study (EPICS), an industry-sponsored trial, compared treatment with finasteride or dutasteride for 12 months [43]. The primary outcome reported, reduction in prostate volume, was not significantly different for the two drugs, although this outcome may not have clinical significance. The drugs were also not significantly different in the secondary endpoints of urinary flow rate and urinary symptom scores, and adverse effects were similar.
The 5-alpha-reductase inhibitors are more effective in men with larger prostates, and their effects on acute urinary retention and reduction in need for surgery require chronic treatment for more than a year.

Dosing — Unlike with alpha antagonists, dosing with 5-alpha-reductase inhibitors do not require titration. Finasteride can be initiated and maintained at 5 mg once daily. Similarly, dutasteride can be initiated and maintained at 0.5 mg once daily.

Side effects — The major side effects of these drugs are decreased libido and ejaculatory or erectile dysfunction. These occurred in 4 to 6 percent of men in a randomized trial of finasteride [33]. Rates of sexual dysfunction in a primary care trial of finasteride were somewhat higher (13.8 percent for any sexual adverse event) [44], and this may be more reflective of clinical practice. However, in a long-term trial of finasteride versus placebo in 3040 men with BPH, adverse sexual effects were increased only during the first year of therapy [45].

Serum prostate-specific antigen (PSA) concentrations decrease by about 50 percent [33], a change that must be kept in mind in interpreting the results of serum PSA measurements in men treated with this drug [46]. Findings from the Prostate Cancer Prevention Trial suggest that PSA values be corrected by a factor of 2 for the first 24 months of finasteride use, and by a factor of 2.5 for longer term use [47]. (See “Measurement of prostate specific antigen”, section on ‘Benign prostatic hyperplasia’.)

Finasteride does not cause loss of bone [48], perhaps because serum estradiol concentrations do not change. A case-control study found no positive association between use of finasteride and hip fracture, and actually found some evidence of lower risk of fracture with finasteride use [49].

In randomized trials, 5-alpha-reductase inhibitors significantly decrease the incidence of prostate cancer. However, concern has been raised about whether 5-alpha-reductase inhibitors increase the incidence of high-grade lesions, although many believe this finding is spurious. This is discussed in detail separately. (See “Chemoprevention strategies in prostate cancer”, section on ‘5-Alpha reductase inhibitors’.)

The United States Food and Drug Administration (FDA) recommends that before starting 5-alpha reductase inhibitors for treatment of BPH, the patient should be assessed for other urological conditions, including prostate cancer [50]. This advisory from the FDA emphasizes the need to monitor these patients for prostate cancer and to recognize the effect that these drugs have on PSA levels. (See “Clinical presentation and diagnosis of prostate cancer” and “Clinical manifestations and diagnostic evaluation of benign prostatic hyperplasia”.)

Discontinuation — Few studies have examined what happens when 5-alpha-reductase inhibitor therapy is discontinued after a course of therapy in men with BPH/LUTS. Most commonly, such therapy is continued indefinitely.

One study that examined this issue involved observational follow-up of a randomized trial that compared one year of therapy with either finasteride or dutasteride in men on ongoing alpha blocker therapy; prostate volume and symptoms were monitored after discontinuation of therapy [51]. At one year after discontinuation, prostate volume had increased 19 to 21 percent, and symptom scores had worsened.

Combination therapy — Short-term therapy with combined alpha adrenergic antagonist and 5-alpha-reductase inhibitor therapy appears to be superior to either agent alone in men with BPH/LUTS and larger prostate glands [52], but not in men with only moderate BPH [53-55]. Long-term combination therapy provides some added benefit even in men with moderate BPH [56].

Short-term efficacy — In the Veterans Affairs Cooperative Study, 1229 men with BPH (mean peak urinary flow rate of 10.5 mL/sec) were randomly assigned to placebo, finasteride (5 mg/day), terazosin (10 mg/day), or both for one year [53]. Eligibility was based upon an American Urological Association symptom score of at least eight, a maximal urinary flow rate of no more than 15 mL/sec, and a residual urine volume of less than 300 mL; prostate size was not a factor. The following results were noted:

- Terazosin lowered the symptom score and increased the peak urinary flow rate when compared with placebo.
- Finasteride alone was no better than placebo.
- The combination of finasteride and terazosin was no better than terazosin alone.

Similar findings were noted in the PREDICT trial in which 1095 men were randomly assigned to doxazosin, finasteride, or both for one year [55]. Doxazosin was more effective than finasteride or placebo for urinary symptoms and flow rate, but again, the combination was no more effective than doxazosin alone.

The mean prostate volume in these studies was approximately 37 mL [53,55], lower than the mean volume of approximately 60 mL in the Finasteride Study Group trial of finasteride alone [33].

Long-term efficacy — Randomized trials have found that long-term combination therapy is superior to single-drug therapy for BPH symptoms [56-57].

The efficacy of long-term therapy was evaluated in the Medical Therapy of Prostatic Symptoms (MTOPS) trial, in which 3047 men with BPH were randomly assigned to receive doxazosin, finasteride, or placebo [56]. Mean prostate volume was 36±20 mL. The patients were evaluated for symptomatic improvement and overall clinical disease progression, defined as an increase above baseline of at least four points in the AUA symptom score, acute urinary retention, urinary incontinence, renal insufficiency, or recurrent urinary tract infection. Long-term combination therapy lowered the risk of overall clinical progression of BPH significantly more than treatment with either drug alone. In addition, combination therapy or finasteride alone (but
not doxazosin alone) reduced the risk of acute urinary retention and the need for invasive therapy.

At a mean follow-up of 4.5 years, the following results were seen (figure 3):

- The risk of overall clinical progression was reduced to a similar degree by doxazosin and finasteride (39 and 34 percent, respectively, when compared to placebo).
- Combination therapy reduced the risk of clinical progression by 66 percent, significantly greater than with either drug alone.
- Symptom scores improved with all therapies, but to a greater degree with combined therapy.
- Combination therapy or finasteride alone (but not doxazosin alone) reduced the risk of acute urinary retention and the need for invasive therapy.
- The number needed to treat to prevent one instance of overall clinical progression was 8.4 for combination therapy, 13.7 for doxazosin, and 15.0 for finasteride.
- Adverse effects were similar with combination therapy and monotherapy, with the exception of abnormal ejaculation, peripheral edema, and dyspnea, which were more common with combination therapy. Breast cancer risk was not increased in the finasteride-only or combination therapy groups.
- A systematic review of the literature concluded that the combination of doxazosin and finasteride compared with doxazosin alone improves urinary symptoms in men with medium (25 to <40 mL) and large (>40 mL) prostates in the long-term.

The four year CombAT study provides additional evidence that combination therapy is effective in men with larger prostates. CombAT included men with BPH age 50 or older, an IPSS of at least 12, a prostate volume ≥30 mL, a PSA ≥1.5 to 10 ng/mL, and a maximum urinary flow rate >5mL and ≤15/second. Subjects were randomly assigned to therapy with dutasteride, tamsulosin, or both; there was no double placebo arm. Mean prostate volume in the 4844 men studied was approximately 55 mL. Combination therapy was superior to tamsulosin monotherapy, but not dutasteride monotherapy, in reducing the relative risk of acute urinary retention or BPH-related surgery. Combination therapy also was superior to either monotherapy in reducing BPH symptoms and the relative risk of BPH clinical progression (figure 3). However, more drug-related adverse events were seen with combination therapy than with monotherapy. Dutasteride alone or in combination with tamsulosin reduced the number of prostate biopsies by 40 percent and the relative risk of prostate cancer by 40 percent in men.

Antimuscarinics — Some men with BPH/LUTS may also have frequency, urgency, and incontinence related to an overactive bladder. Bladder contractions are stimulated by acetylcholine effects on muscarinic receptors in smooth muscle of the bladder. A randomized trial in patients with moderate to severe obstructive symptoms, at least a moderate bother score, and urgency found that combination therapy with an anticholinergic agent with antimuscarinic effects (tolterodine) plus an alpha-1-adrenergic antagonist (tamsulosin) was reasonably safe with few episodes of urinary retention. There was some suggestion that combination therapy was more effective than tamsulosin alone. Use of antimuscarinic agents should be restricted to men with low post-void residual volumes. (See "Lower urinary tract symptoms in men").

Herbal therapies — Herbal therapies for BPH are commonly used in Europe; these remedies comprised 70 percent of spending for drug treatment of prostatism in Germany in 1997. Saw palmetto is approved by the German Commission E for stage I and II (mild to moderate) BPH. Two herbal extracts have officially been approved for the treatment of prostatism in France. No herbal therapies have been approved by the United States Food and Drug Administration for this purpose, although many men probably try these treatments. There is a substantial placebo effect associated with herbal therapy, as there is for most drugs used to treat BPH.

The data concerning efficacy of these therapies are conflicting. In systematic reviews of controlled trials, saw palmetto plant extract was as effective as finasteride in relieving the symptoms of prostate obstruction, although it did not decrease prostate volume. A subsequent placebo-controlled trial found no evidence that saw palmetto was superior to placebo. The evidence regarding the use of saw palmetto for BPH is discussed in detail separately. (See "Clinical use of saw palmetto").

There is some evidence for efficacy of other agents as well. Systematic reviews have suggested the following:

- The plant extract beta-sitosterol improved symptoms.
- Cernilton, which is prepared from the rye grass pollen, Secale cereale, has been evaluated in four clinical trials. It improved symptoms, but did not affect urinary flow rates or residual urine or prostate volume.
- Pygeum africanum is an extract of bark from an African plum tree. In a meta-analysis of 18 randomized controlled trials, active treatment improved symptoms two times more frequently than placebo and increased peak urinary flow rates 23 percent.

Despite these systematic reviews, questions regarding safety and efficacy remain. As has been seen with saw palmetto (see "Clinical use of saw palmetto"), better designed trials do not always confirm the favorable results seen in less well-designed studies. Additionally, questions regarding standardization remain, particularly in the US. (See "Overview of herbal medicine and dietary supplements").

Until additional studies of herals are performed, we suggest using alpha-adrenergic antagonists and 5-alpha-reductase inhibitors rather than any of the above herbal therapies.
Medical treatment of benign prostatic hyperplasia

Other — Observational studies suggested that phosphodiesterase-5 (PDE-5) inhibitors, primarily used as treatments for erectile dysfunction, were beneficial for BPH/LUTS [66] and led to subsequent clinical trials. In a meta-analysis of five randomized trials of men with LUTS secondary to BPH, PDE-5 inhibitors led to significant improvement in IPSS after ≥12 weeks of therapy, compared to placebo [67]. There was no significant difference in urodynamic parameters. A report found maximum urine flow rates as well as symptom scores to be improved by daily tadalafil [68]. The long-term effect of PDE-5 inhibitors in patients with BPH is unclear. Tadalafil is approved by the US Food and Drug Administration for use in BPH. It seems reasonable to discuss this option with men who have erectile dysfunction and mild or moderate symptoms of BPH. Daily dosing of tadalafil should not be prescribed in men with a creatinine clearance <30 mL/min.

As discussed above, PDE-5 inhibitors can potentiate the hypotensive effects of alpha-1-adrenergic antagonists. (See ‘Side effects and interactions’ above.)

There is some evidence that nonsteroidal antiinflammatory drugs (NSAIDs) can reduce symptoms of BPH/LUTS without improving urine flow rates [69].

MODIFICATION OF THERAPY — Patients who experience side effects with either alpha-adrenergic antagonists or 5-alpha-reductase inhibitors can reasonably be switched to the other agent. Patients who have obstructive symptoms on an alpha-adrenergic antagonist may be candidates for antimuscarinic treatment if they have low post-void residual volumes, and patients who do not tolerate any of these therapies can be observed off therapy or can be referred for invasive therapy.

Patients who are on combination therapy and do not experience an adequate response over 12 to 24 months may wish to consider invasive therapies as well. Patients with progression of disease on therapy will generally require invasive therapy. (See "Surgical and other invasive therapies of benign prostatic hyperplasia".)

OTHER STRATEGIES — Patients with BPH/LUTS should avoid medications that can exacerbate symptoms or induce urinary retention. These include anticholinergic medications such as sedating antihistamines and adrenergic agents such as decongestants.

Behavioral modifications may be helpful. These include avoiding fluids prior to bedtime or before going out, reducing consumption of mild diuretics such as caffeine and alcohol, and double voiding to empty the bladder more completely.

A randomized trial found that, compared with men followed with watchful waiting alone, men given an educational intervention that included teaching of behavioral modifications were significantly less likely to experience treatment failure (mainly an increase in IPSS or requirement for medication) [70].

ECONOMIC CONSIDERATIONS — Management of BPH/LUTS is estimated to cost more than $4 billion per year in the United States [71]. While the short-term costs of medical treatment are less than those of invasive treatment, many have questioned whether invasive treatment might be less expensive in the long run.

One study that examined this question in 970 privately insured men concluded that surgery was associated with higher costs and failure rates over a five year period, and medical therapy remained less expensive than invasive therapy over the long term [72].

INFORMATION FOR PATIENTS — UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics."

The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on “patient info” and the keyword(s) of interest.)

- Basics topics (see "Patient information: Benign prostatic hyperplasia (enlarged prostate) (The Basics)"
- Beyond the Basics topics (see "Patient information: Benign prostatic hyperplasia (BPH) (Beyond the Basics)"

SUMMARY AND RECOMMENDATIONS

- Benign prostatic hyperplasia (BPH) becomes increasingly common as men age. BPH can lead to urinary symptoms that may benefit from medical or surgical treatment. However, many men with BPH are asymptomatic or have only mild symptoms and may not require therapy. Additionally, many men with symptoms will improve or stabilize without therapy. (See ‘Introduction’ above and ‘Indications for therapy’ above.)
- In general, men who develop upper tract injury (eg, hydronephrosis, renal dysfunction) or lower tract injury (eg, urinary retention, recurrent infection, bladder decompensation) require invasive therapy. (See "Surgical and other invasive therapies of benign prostatic hyperplasia".)
- We suggest that men with symptoms of BPH be instructed in behavior modifications (Grade 2B). These should be tailored to symptoms but may include avoiding fluids prior to bedtime or before going out, reducing consumption of mild diuretics such as caffeine and alcohol, and double voiding to empty the bladder more completely. (See ‘Other strategies’ above.)
- Alpha-adrenergic antagonists provide immediate therapeutic benefits, while 5-alpha-reductase inhibitors require long-term treatment for efficacy. In most men with mild to moderate symptoms of BPH where those symptoms have a sufficient effect on quality of life that they desire therapy, we suggest initial treatment with an alpha-adrenergic antagonist alone (Grade 2A). In men with severe symptoms, those with a large prostate (>40 g), and in those who do not get an adequate response to maximal dose monotherapy with an alpha-adrenergic antagonist, we suggest combination treatment with an alpha-adrenergic antagonist and a 5-alpha-reductase inhibitor (Grade 2A). (See 'Combination therapy' above.)

- The choice of alpha-adrenergic antagonist and 5-alpha-reductase inhibitor may be made on the basis of cost and side-effect profile. Tamsulosin, alfuzosin, and silodosin have less effect on blood pressure than either terazosin or doxazosin, and tamsulosin may further have slightly less effect on blood pressure than alfuzosin. (See 'Alpha-1-adrenergic antagonists' above.)

  The two 5-alpha-reductase inhibitors, finasteride and dutasteride, appear to have similar efficacy and similar adverse effects. The agents are more effective in men with larger prostates, and their effects on acute urinary retention and reduction in need for invasive therapies require chronic treatment for more than a year. (See '5-alpha-reductase inhibitors' above.)

- In men with low post-void residual urine volumes and irritative symptoms (eg, frequency, urgency) that persist during treatment with an alpha-adrenergic antagonist, we suggest treatment with an antimuscarinic agent (Grade 2B). Side effects may be minimized by using a low dose of short-acting medications (eg, tolterodine 1 mg twice daily). Alternatives include extended-release tolterodine, M3 selective drugs (eg, darifenacin, solifenacin), or quaternary amines (eg, trospium). (See 'Antimuscarinics' above and "Lower urinary tract symptoms in men".)

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Prevalence of benign prostatic hyperplasia pathology with age

Age-associated increase in pathologic evidence of benign prostatic hyperplasia in 1075 men at autopsy. The percentage with benign prostatic hyperplasia was determined during 10-year intervals from five different studies; the mean values are shown.

## International Prostate Symptom Score (IPSS)

<table>
<thead>
<tr>
<th>Questions to be answered</th>
<th>Not at all</th>
<th>Less than 1 time in 5</th>
<th>Less than half the time</th>
<th>About half the time</th>
<th>More than half the time</th>
<th>Almost always</th>
<th>Your score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>2. Over the past month, how often have you had to urinate again less than 2 hours after you finished urinating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>3. Over the past month, how often have you found you stopped and started again several times when you urinated?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>4. Over the past month, how often have you found it difficult to postpone urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>5. Over the past month, how often have you had a weak urinary stream?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>6. Over the past month, how often have you had to push or strain to begin urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>7. Over the past 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?</td>
<td>0 (none)</td>
<td>1 (1 time)</td>
<td>2 (2 times)</td>
<td>3 (3 times)</td>
<td>4 (4 times)</td>
<td>5 (5 or more times)</td>
<td></td>
</tr>
</tbody>
</table>

**Sum of numbers (AUA symptom score):**
### Total score:
- 0 to 7: Mild symptoms
- 8 to 19: Moderate symptoms
- 20 to 35: Severe symptoms

<table>
<thead>
<tr>
<th>Quality of life due to urinary symptoms</th>
<th>Delighted</th>
<th>Pleased</th>
<th>Mostly satisfied</th>
<th>Mixed - about equally satisfied and unsatisfied</th>
<th>Mostly dissatisfied</th>
<th>Unhappy</th>
<th>Terrible</th>
</tr>
</thead>
<tbody>
<tr>
<td>If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

## Alpha-1 receptor antagonist for BPH*

### Dose titration schedule to reduce orthostatic effects[1]

<table>
<thead>
<tr>
<th>Terazosin standard (appropriate for most patients)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Days 1 to 3</td>
<td>1 mg</td>
</tr>
<tr>
<td>Days 4 to 14</td>
<td>2 mg</td>
</tr>
<tr>
<td>Weeks 2 to 6</td>
<td>5 mg</td>
</tr>
<tr>
<td>Weeks 7 and thereafter</td>
<td>10 mg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Terazosin rapid (for selected patients)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Days 1 to 3</td>
<td>1 mg</td>
</tr>
<tr>
<td>Days 4 to 14</td>
<td>2 mg</td>
</tr>
<tr>
<td>Weeks 2 to 3</td>
<td>5 mg</td>
</tr>
<tr>
<td>Weeks 4 and thereafter</td>
<td>10 mg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Doxazosin (immediate release)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Days 1 to 3</td>
<td>1 mg</td>
</tr>
<tr>
<td>Days 4 to 14</td>
<td>2 mg</td>
</tr>
<tr>
<td>Weeks 2 to 6</td>
<td>4 mg</td>
</tr>
<tr>
<td>Weeks 7 and thereafter</td>
<td>8 mg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Doxazosin (extended release preparation only)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Days 1 to 21</td>
<td>4 mg</td>
</tr>
<tr>
<td>Week 4 and thereafter</td>
<td>8 mg</td>
</tr>
</tbody>
</table>

### Uroselective Alpha-1 receptor antagonists[2]

#### Alfuzosin
- Initial and maintenance: 10 mg

#### Tamsulosin
- Initial and maintenance: 0.4 mg
- If inadequate response after 2-4 weeks: 0.8 mg

#### Silodosin
- Initial and maintenance: 8 mg

---

BPH: benign prostatic hyperplasia.

* Titrate dose as tolerated and as needed for effect. Oral administration for all medications is once daily at bedtime. Peak effect of a given dose on BPH symptoms may not be fully evident until 4 to 6 weeks. If therapy is interrupted for three or more days, reinitiate at lowest dose and re-titrate according to schedule.

• Due to lower risk of orthostatic hypotension and syncope, uroselective agents do not require gradual dose titration. Oral administration for all medications is once daily at bedtime.


Finasteride reduces surgery and acute urinary retention in BPH

Effect of finasteride (5 mg/day) versus placebo on the probability of surgery and acute urinary retention in 3016 men with moderate to severe benign prostatic hyperplasia. Both endpoints were significantly (P<0.001) reduced in the men treated with finasteride.

Combination therapy for benign prostatic hyperplasia

Mean adjusted change in International Prostate Symptom Score (IPSS) from baseline by visit and treatment group.

* p<0.001 for combination versus dutasteride.
§ p<0.001 for combination versus tamsulosin.

Reproduced from: Roehrborn CG, Siami P, Barkin J, et al. The effects of combination therapy with dutasteride and tamsulosin on clinical outcomes in men with symptomatic benign prostatic hyperplasia: 4-year results from the CombAT study. Eur Urol 2010; 57:123. Illustration used with the permission of Elsevier Inc. All rights reserved.