Disorders of the prostate (benign hyperplasia and adenocarcinoma) account for a high proportion of visits to urologists by men over 50. The prostate is a structure about the size of a walnut that surrounds the urethra just below the neck of the bladder. Both the prostate and the seminal vesicles (small sac-like glands adjacent to the spermatic duct) produce a fluid secretion that contributes to the composition of semen. Smooth muscle fibers in the prostate contract at the time of ejaculation, preventing retrograde flow of semen into the bladder.

Benign prostatic hyperplasia (BPH) is an overgrowth of androgen-sensitive glandular tissue that normally accompanies aging. The disorder may remain asymptomatic for years, but most elderly men eventually experience both irritative and mechanical effects. Irritative symptoms result from an heightened sensitivity in the neck of the bladder and prostatic urethra, and include pollakiuria (increased urinary frequency), urgency, nocturia (the need to get up one or more times at night to urinate), and burning or stinging on urination. Mechanical symptoms arise from distortion of urethral anatomy by prostatic swelling. Compression of the urethra causes hesitancy (difficulty in starting urination), reduction in the force and volume of the urinary stream, inadequate emptying of the bladder, and difficulty in stopping urination (postvoiding dribbling). Recurrent failure to empty the bladder completely can lead to chronic distention and overflow incontinence.

Occasionally the presenting symptom of BPH is acute urinary retention, requiring prompt catheterization to relieve distress and prevent complications such as hydronephrosis (filling of the ureters and renal pelves with urine under pressure) and urinary tract infection. The diagnosis of BPH is based on history, palpation of the gland by digital rectal examination, and the performance of various procedures to rule out cancer (discussed below).

Benign enlargement of the prostate is typically symmetrical (not nodular), and the gland feels firm but not stony hard. The examining finger can reach only the posterior lobe of the prostate and most of the right and left lateral lobes. Enlargement of these parts of the gland doesn’t necessarily correlate with the degree to which urine flow is compromised by the anterior and median lobes.

Catheterization of the bladder immediately after voiding may yield a substantial volume of retained urine (“postvoiding residual”). Other diagnostic procedures sometimes used include endoscopy (examination of the prostatic urethra with a urethroscope or cystoscope) and voiding cystourethrography (VCUG), a radiographic study of the bladder and urethra during voiding after injection of contrast medium through a catheter.

The symptoms of benign prostatic hyperplasia often respond to oral medicines. Two major classes of prescription drug, 5α-reductase (5-alpha-reductase) inhibitors and α-1 (alpha-1) adrenergic blockers, are currently approved for this indication.

In order to exert its physiologic effects, testosterone must be converted to its active form, dihydrotestosterone, by the enzyme 5α-reductase. Drugs that inhibit that enzyme reduce the formation of dihydrotestosterone and thus reverse prostatic hyperplasia, which is hormone-dependent. The two 5α-reductase inhibitors currently approved are dutasteride (Avodart) and finasteride (Proscar). (Finasteride is also marketed under the
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trade name Propecia for the treatment of male-pattern baldness, which is also dependent on dihydrotestosterone.) The 5α-reductase inhibitors reduce gland bulk very slowly, and weeks or months of treatment may be needed before results are seen. Possible side effects of these agents are diminished libido, erectile dysfunction, and breast swelling and tenderness. Finasteride and dutasteride can also delay the diagnosis of prostatic carcinoma by lowering the serum level of prostate specific antigen (PSA), to be discussed below.

Alpha-1 adrenergic blockers are the other class of prescription drug currently used to treat BPH: alfuzosin (Uroxatral), doxazosin (Cardura), prazosin (Minipress), tamsulosin (Flomax), and terazosin (Hytrin). These agents improve urinary flow by relaxing smooth muscle in the prostate gland. Beneficial effects are often noted within a day or two of starting treatment, but because alpha-1 blockers don’t reduce the bulk of the prostate, they may provide little relief for men with very large glands. Alpha-1 blockers were originally developed to treat hypertension. Doxazosin, prazosin, and terazosin are among drugs in this class that are currently approved for lowering blood pressure. Dizziness, light-headedness, and orthostatic hypotension (a symptomatic drop in blood pressure on standing up from a sitting or reclining position) are experienced fairly often by men taking alpha-1 blockers for prostatic hyperplasia.

Some physicians routinely prescribe a drug from each class. A combination product called Jalyn contains both dutasteride and tamsulosin. Saw palmetto (Serenoa repens) is a small New World palm whose leaf stems (petioles) are edged with sharp spines, hence its name. Extracts of its edible fruit have been used for centuries in folk medicine for a variety of indications, including urologic disorders. In controlled clinical trials, saw palmetto has performed better than placebo in improving urine flow in BPH and has matched the effects of prescription medicines in mild disease. It has also yielded promising results in male-pattern baldness. Limited pharmacologic studies suggest that it has both alpha-1 blocking and alpha-reductase inhibiting properties. Saw palmetto extract, being a natural product, ranks as a nutraceutical and is thus essentially exempt from oversight by the United States Food and Drug Administration (FDA). It has not been approved by the FDA for any indication, and standards of purity have not been established for it. Available formulations may therefore vary widely in both efficacy and safety.

A generation ago, symptomatic prostatic hyperplasia was routinely managed by various surgical procedures, including total excision of the gland. More recently, the availability of effective oral medicines has greatly reduced the frequency of surgery for this indication. Surgery is still considered appropriate for men with severe disease refractory to drug treatment, those for whom drugs are contraindicated, and those with certain complications (recurrent acute obstruction, frequent urinary tract infections, hydronephrosis, bladder stones, hematuria).

For selected patients, prostatectomy (removal of the entire gland) is considered the procedure of choice. The surgeon may use either a perineal or a retropubic approach to the gland. In the latter technique, an incision is made in the lower abdomen and the bladder is dissected free from the anterior abdominal wall. Healing time after either procedure is prolonged, and postoperative complications such as incontinence and sexual dysfunction are relatively common.

For many years the standard surgical technique for BPH has been transurethral resection of the prostate (TUR, TURP). Under spinal or general anesthesia, a modified endoscope called a resectoscope is inserted through the penis and advanced to the level of the hyperplastic prostate. The surgeon then shaves away surplus tissue encroaching on the lumen of the urethra by means of an electrical loop, which also seals severed blood vessels. The instrument is equipped with an irrigating system that flushes away blood and tissue.

Obviously this technique also removes the mucosal lining of the prostatic urethra, which takes weeks to heal completely. An irrigating catheter remains in the bladder for about 72 hours after surgery. Mild to severe stress incontinence (leakage of urine with coughing, laughing, or straining), enuresis (bedwetting), and hematuria, often with passage of clots, may persist for several days.

About one third of patients experience some degree of sexual dysfunction after TURP, at least temporarily. Retrograde ejaculation (passage of semen into the bladder during orgasm) results from replacement of prostatic periurethral smooth muscle by scar tissue and is usually permanent. Because TURP removes only part of the gland, it is not as definitive a treatment as prostatectomy. Obstructive symptoms can recur after TURP and may require periodic repetitions of the procedure.

Several modifications of TURP have been devised to reduce the incidence and severity of complications and to shorten healing time. In transurethral incision of the prostate (TUIP), longitudinal incisions are made in the prostatic urethra without removal of any tissue. The risk of retrograde ejaculation is less after this type of surgery, but long-term control of symptoms has not been demonstrated.

Holmium laser enucleation of the prostate (HoLEP) uses a holmium laser to resect hyperplastic tissue instead of the electrical loop of traditional TURP. In holmium laser ablation of the prostate (HoLAP), surplus tissue is vaporized rather than trimmed away. Transurethral ultrasound-guided laser incision of the prostate (TULIP) resembles TUIP, but the incisions are made with a laser. One of the latter two techniques may suffice when the total volume of the prostate is relatively small. Bleeding during and after surgery is less with laser procedures, which can usually be performed as outpatient surgery.
Still less damaging methods use lasers or microwave radiation to coagulate excessive prostatic tissue. These are brief office procedures with few adverse effects or complications, but long-term outcomes may not match those of more aggressive measures. The most conservative and least invasive procedure for BPH is placement of a metal stent within the prostatic urethra through an endoscope under regional anesthesia. This procedure can be performed in patients with medical conditions that forbid more elaborate surgery. However, adverse effects (dysuria, pollakiuria, incontinence) often occur. The removal of a prostatic stent, which may be deemed necessary in as many as one third of patients, often proves more difficult and invasive than its insertion.

**Adenocarcinoma of the prostate** is the most common cancer in men and the second most common cause of cancer deaths in men (after lung cancer). A carcinoma is a malignant tumor arising from epithelial tissue; an adenocarcinoma arises from glandular epithelium. Like BPH, prostate cancer represents an overgrowth of hormone-sensitive secretory cells in the prostate. There the similarities end. BPH is by definition benign, while prostatic carcinoma is malignant. BPH does not evolve or degenerate into cancer.

Prostate cancer is more common, occurs at an earlier age, and spreads more aggressively in African American men. Because malignant changes usually begin near the periphery of the gland, urinary symptoms occur late, if at all. In more than one third of patients, cancer has spread beyond the gland by the time the diagnosis is made. Prostate cancer can invade the bladder, rectum, and other pelvic structures by direct extension and can spread to more remote sites by metastasis. The bones of the spine and pelvis are the most frequent sites of metastasis.

Nowadays, the diagnosis is usually made when the screening of an apparently healthy man by means of **digital rectal examination** (DRE) or determination of the serum level of **prostate specific antigen** (PSA) yields abnormal results. An asymmetrically enlarged or nodular prostate, or one that feels abnormally hard to the examining finger, suggests the presence of malignancy. Although rectal palpation of the prostate is easily performed, requires no special preparation, and causes little discomfort, the procedure has low sensitivity (below 25% in some studies) and even lower specificity (below 10% in some studies).

**Prostate specific antigen**, an enzyme that helps to maintain the fluidity of semen, is produced by the secretory epithelium of the prostate. (Trace amounts occur in other tissues, including the endometrium and the female breast.) A level below 2 ng/mL (2 mcg/L) appears in the blood of normal men. Elevation of the serum concentration of PSA is highly organ-specific, reliably drawing attention to the prostate, but is not at all disease-specific.

Statistically, most elevations above 4 ng/mL are due to prostatitis, not cancer. Other causes of elevation include benign prostatic hyperplasia, prostatic infarction, recent ejaculation, and even digital examination of the prostate. As many as one third of elevated PSA levels return to normal on followup testing without treatment. Although a level above 9 ng/mL (9 mcg/L) strongly suggests cancer, the PSA level is normal in more than 10% of men with biopsy-proven cancers.

Despite these limitations, the test was hailed as a more sensitive and more specific means of detecting early cancer than digital rectal examination when it was first approved by the FDA in 1992. Both the American Cancer Society and the American Urological Association recommended routine annual PSA screening as well as digital rectal examination for men over 50 (over 40 for African American men or those with a family history of prostate cancer). After a brief show of resistance, Medicare began covering the cost of one PSA screening per year, and continues to do so. By the end of the twentieth century, PSA screening had become part of the standard of care for men over 50.

But almost from the first, the routine use of **PSA testing in asymptomatic men has been the subject of intense controversy**. A remarkable increase in the reported incidence of prostatic carcinoma during the 1990s seemed to confirm the value of PSA screening. But it quickly became evident that the test was yielding an unacceptably high level of false positive and false negative results. A false positive test for prostate cancer causes needless anguish and expense and often leads to unnecessary treatment. Conversely, a false negative result from this highly touted procedure can generate an erroneous conviction that one is free of cancer, and can delay diagnosis until the disease has reached an advanced stage.

The lack of both sensitivity and specificity for prostate cancer is an inherent and irremediable deficiency of **PSA screening**. Lowering the cutoff level between normal and abnormal PSA increases the chance of detecting cancer at the expense of increasing the rate of false-positive results. Efforts to enhance the value of the test by modifying the procedure or its interpretation have included determination of PSA velocity (rate of change in PSA level with the passage of time), age-adjusted PSA (using higher cut-off levels for older men), PSA density (the ratio of PSA level to the size of the prostate), and the ratio of free to protein-bound PSA (lower in malignant disease). None of these has shown clear-cut benefits in large statistical studies.
Many prostate cancers grow very slowly and never cause symptoms. Indeed, foci of cancer are found in the prostates of 40% of men dying of other causes after age 50. PSA screening, by detecting many small cancers that would never become life-threatening, subjects some patients to basically futile treatment that may have adverse effects such as urinary incontinence and erectile dysfunction.

The 10-year survival rate of diagnosed prostatic carcinoma is about 90%. For that reason, virtually all authorities now oppose routine periodic digital rectal examination and PSA screening of asymptomatic men with life expectancies of less than 10 years, on the grounds that the risks of false positive results and of adverse consequences of aggressive treatment outweigh any possible benefit in survival or quality of life.

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The American College of Preventive Medicine has concluded that there is insufficient evidence to recommend routine screening with either DRE or PSA in men of any age. Both the U.S. Preventive Services Task Force and the National Cancer Institute advise against routine PSA testing.

Suspicion of prostatic carcinoma, whether based on symptoms or on abnormal results of screening, is followed up by biopsy of the gland. Prostatic biopsy is usually performed in conjunction with a transrectal ultrasound (TRUS) examination to assess the size and configuration of the gland. Under ultrasonic guidance, the examiner secures specimens from 10 or more sites with a spring-loaded biopsy needle that enters the gland and extracts a core of tissue in a fraction of a second.

Routine preparation for this procedure includes a cleansing enema, increased fluid intake to distend the bladder, prophylactic antibiotics, and local anesthesia. Alternative methods, less often used, obtain tissue through a perineal incision or through an endoscope inserted into the urethra. Adverse effects include pain, infection, and bleeding in urine, semen, or stool.

If sampled tissue is cancerous, microscopic examination shows cellular changes characteristic of malignancy, including varying degrees of anaplasia—a lack of the cellular differentiation that is typical of normal prostate tissue. Anaplasia is graded on a scale of 1 (nearly normal glandular differentiation) to 5 (total lack of differentiation). The Gleason score (developed about 40 years ago by the American pathologist Donald F. Gleason) has been found useful in converting biopsy findings into prognostic information and in planning treatment. This score is determined by simply adding the grades of the two least differentiated specimens. A Gleason score of 2 or 3 is associated with a relatively favorable prognosis, a score of 9 or 10 with a poor prognosis.

The secretory cells of the prostate are highly sensitive to hormonal stimulation by testosterone. Neither BPH nor adenocarcinoma of the prostate occurs in eunuchs (men without testicles). Measures that reduce or block androgenic stimulation of cancer cells can slow the progression of the primary tumor and suppress growth of metastases. Antiandrogen therapy is often indicated in both early and advanced disease.

The most drastic and definitive means of stopping hormonal stimulation of prostate cancer is bilateral orchiectomy (castration, removal of both testicles). Pharmacologic agents often used are the androgen receptor blocker flutamide (Eulexin, Flutamin) and the gonadotropin-releasing hormone (GnRH) agonist leuprolide (Eligard, Lupron, Viadur).

Surgical procedures for advanced or highly malignant prostatic carcinoma include radical prostatectomy, which is associated with a considerable risk of urinary incontinence and erectile dysfunction, external x-ray or proton beam radiation, and transperineal implantation of radioactive isotopes.