Prostate Cancer:

A Primer for Health-System Pharmacists
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Accreditation

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Program Description and Intended Audience

This monograph has been developed for pharmacists in an acute care environment who wish to expand their knowledge of prostate cancer.

Learning Objectives

After successfully completing this program, participants should be able to do the following:

# List the risk factors for prostate cancer.
# Describe the incidence and mortality associated with this malignancy.
# Describe the pathologic features and symptoms of prostate cancer.
# Compare and contrast the symptoms of prostate cancer with benign prostatic hyperplasia.
# Review the diagnostic and screening methods for prostate cancer.
# Compare the different stages of prostate cancer as defined by the TNM Staging System.
# Contrast the various treatment options: surgery, radiation, hormone therapy, and chemotherapy.
# Discuss recommendations for treatment made by the National Comprehensive Cancer Network.

Directions for Program Completion
[[insert]]
INTRODUCTION

As prominent prostate-cancer survivors have come forward to tell their inspirational stories, more attention than ever before is directed toward this disease. Advances in the screening, diagnosis, and management of prostate cancer have occurred over the last decade, yet the mortality rate for this disease has remained relatively unchanged.\(^1\) Clearly there is still a long way to go to beat prostate cancer, but new therapies and preventative strategies will help. Diet, family history, and ethnicity have become important factors in guiding treatment decisions.

This primer was designed to familiarize the hospital pharmacist with the basic facts about prostate cancer. This includes an understanding of the incidence of prostate cancer and its risk factors, diagnosis, and staging. The therapeutic modalities and treatment strategies will also be reviewed.
INCIDENCE & EPIDEMIOLOGY

Prostate cancer is the most commonly diagnosed cancer in men, excluding skin cancer. In 1999, an estimated 179,300 men in the United States alone have been diagnosed with prostate cancer. Among men it is exceeded only by lung cancer in its ferocity, claiming 37,000 lives in 1999. In the United States, a man’s lifetime risk of developing prostate cancer is 1 in 6, compared with a 1 in 2 lifetime risk of developing any kind of cancer. *Lifetime risk* is the chance that a person will develop cancer over his or her entire life.²

**Risk Factors**

**Age.** The most important risk factor for prostate cancer is age.³ At least 75% of the men who will be diagnosed with prostate cancer this year are over the age of 65 years.² In males under the age of 40, the risk of prostate cancer is less than 1 in 10,000, but in men in their 60s and 70s, the risk climbs to 1 in 7.² In fact, it has been estimated that 70% of men over 80 years of age have some prostatic cellular changes that suggest cancer (*histologic cancer*).³ This does not mean, however, that all of these men will go on to show the signs and symptoms of prostate cancer, because about 10% of histologic prostate cancers never advance.³

**Race/ethnicity.** Prostate cancer does not strike all racial and ethnic groups evenly; indeed, African-Americans are more likely to be affected
than any other population. Table 1 shows the incidence and mortality for selected racial and ethnic groups living within the United States.

Table 1

The incidence of prostate cancer also differs among countries in the world. In the United States, the incidence of prostate cancer from 1988 to 1991 was 16.8 per 100,000. During the same time period, the incidence in Norway was 20 per 100,000, in Japan was 3.8 per 100,000, and in Hong Kong was 2.6 per 100,000. This wide variation in incidence among different countries suggests a genetic role, an environmental factor, or both exerting their effects with varying intensity throughout the world.

Diet. Another possible risk factor for prostate cancer is diet. A diet high in saturated fats, especially those found in red meats and butter, increases the risk of prostate cancer by
two to three times. As much as 10% of the difference in the incidence of prostate cancer between African-Americans and Caucasians can be traced to the amount of saturated fats in the diet. Conversely, some substances in the diet may have a protective effect against prostate cancer. Some evidence suggests that the mineral selenium may have a role in lowering the incidence of and mortality from prostate cancer. Lycopene, a natural chemical found in tomatoes, grapefruit, and watermelon, may reduce the risk of prostate cancer.

Genetics. Family history influences the risk of prostate cancer. A man’s prostate cancer risk doubles if he has one first-degree relative (father, brother) with the disease, and quadruples if two or more first-degree relatives have prostate cancer. Nine percent of all prostate cancer cases in the United States are thought to be hereditary. The defective gene(s) that cause prostate cancer have not yet been conclusively identified, and although the genetic abnormalities are probably present in less than 0.5% of men, 90% of men with these genetic flaws will have had prostate cancer by the time they are 80 years old. Cases of breast cancer and prostate cancer in families have been associated with the BRCA1 gene, and further research is needed to clarify the role of this and other genetic influences on prostate cancer.

Hormones. Male sex hormones may be involved in prostate cancer. Another hormone, insulin-like growth factor-1, when present in high concentrations may also increase the risk of prostate cancer. (Insulin-like growth factor-1 is a hormone involved in the regulation of cell growth.)
Vasectomy. No consistent association has been shown between a vasectomy and prostate cancer.³ (A vasectomy renders a man sterile by severing the vas deferens, which connect the testicles to the prostatic urethra, through which semen travels.) Two large studies found a weak association between a vasectomy and the development of prostate cancer, with an attendant small increase in risk. But other studies have failed to demonstrate a link. Clearly, further study is needed to resolve the relationship, if any, between a vasectomy and an increased risk of prostate cancer.⁵

**Survival from Prostate Cancer**

The more advanced the cancer at the time of diagnosis, the less likely the patient is to survive. The majority of prostate-cancer cases are detected at an early stage.

Figure 2 shows a breakdown of the stage at which prostate cancers are diagnosed. When diagnosed at a local or regional stage, prostate cancer is cured 100% and 94.1% of the time, respectively. On the other hand, prostate cancer that is diagnosed at a distant stage is only curable in 30.9% of cases.¹
Furthermore, race has an impact on survival. African-Americans are less likely to be alive five years after the diagnosis of prostate cancer (75% vs 90% survival rates).¹

Review Points

- Prostate cancer is the most commonly diagnosed cancer in men, excluding skin cancer, and the second most common cause of cancer-related death in men over the age of 50 years
- Risk factors include age, race/ethnicity, diet, and hormonal and genetic factors
- 1 in 6 men will develop prostate cancer in their lifetime
- Improved survival odds occur when prostate cancer is diagnosed at an earlier stage
PATHOLOGY OF PROSTATE CANCER

The prostate gland is a walnut-sized organ that encircles the urethra. It secretes a milky substance into the urethra during ejaculation. Pertinent anatomical structures in the male which are related to the prostate gland are shown in Figure 2.

When the prostate gland is cancerous, it is almost always an adenocarcinoma. Other tumor types, such as ductal adenocarcinoma, mucinous adenocarcinoma, small cell, and transitional carcinoma occur rarely.
**Histopathologic Grading**

Histopathologic tumor grades are assigned after a prostate biopsy as follows:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Histopathologic Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>GX</td>
<td>Grade cannot be assessed</td>
</tr>
<tr>
<td>G1</td>
<td>Well differentiated (slight anaplasia)</td>
</tr>
<tr>
<td>G2</td>
<td>Moderately well differentiated (moderate anaplasia)</td>
</tr>
<tr>
<td>G3-4</td>
<td>Poorly differentiated or undifferentiated (marked anaplasia)</td>
</tr>
</tbody>
</table>

Many different histologic grading systems have been used for prostate cancer. The Gleason score has been well accepted, and is featured as part of the National Comprehensive Cancer Network (NCCN)\(^a\) guidelines for prostate cancer. The following are values assigned by the Gleason score through an assessment of the tumor’s histopathologic grade, and the metastatic risk associated with the different Gleason scores.

\(^a\)The NCCN is a consortium of member institutions providing comprehensive cancer care. The NCCN has developed practice guidelines for prostate cancer. These guidelines were updated in 1997. The NCCN’s web site is [http://www.nccn.org/](http://www.nccn.org/).
<table>
<thead>
<tr>
<th>Gleason Score</th>
<th>Histopathologic Assessment</th>
<th>Risk of Metastasis⁶ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 - 4</td>
<td>well differentiated</td>
<td>20</td>
</tr>
<tr>
<td>5 - 7</td>
<td>moderately or moderately poorly</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>differentially</td>
<td></td>
</tr>
<tr>
<td>8 - 10</td>
<td>poorly differentiated</td>
<td>75</td>
</tr>
</tbody>
</table>
DIAGNOSIS AND SCREENING

Diagnostic means for prostate cancer have improved substantially since 1986, when the prostate-specific antigen (PSA) blood test was introduced. This section will review the tools available to health care professionals and the current recommendations for prostate cancer screening.

Diagnostic & Screening Tools

Signs & Symptoms. During a history and physical examination, a physician will inquire about symptoms that, while not specific for prostate cancer, may suggest the need for diagnostic tests. The types of signs and symptoms found in patients with prostate cancer vary, and in the early stages symptoms do not generally arise at all.

Nonspecific symptoms include:

- hematuria
- pain on ejaculation, decrease in or thinning of the semen, blood in the semen
- problems with urination, such as frequent urination, urgency, and incontinence

Digital Rectal Examination (DRE). DRE is performed by a trained health care professional, who inserts a gloved, lubricated finger into the patient’s rectum to detect any irregularity in the accessible area of the prostate gland. The DRE is not painful, but may be uncomfortable. It just takes a few moments to perform, however.
DRE is not specific for prostate cancer, meaning that only 25% to 50% of men with abnormalities detected with DRE will have prostate cancer.\(^3\) It is also important to remember that men with a normal DRE may still have prostate cancer.

Other disease states that must be included in the differential diagnosis with prostate cancer when abnormal findings are evident during DRE are prostatitis and a prostatic calculus.\(^3\) Patients with abnormal DRE results should have a PSA test and/or a biopsy to rule out other diagnoses.

**PSA Blood Test.** PSA is a protein normally produced by the prostate gland. When the PSA level in the blood is elevated, there is a risk of prostate cancer and other prostate conditions as well.

<table>
<thead>
<tr>
<th>If the PSA level is... (^7)</th>
<th>it is considered....</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 4 ng/mL</td>
<td>Normal</td>
</tr>
<tr>
<td>4 to 10 ng/mL</td>
<td>Moderate/suspicious for malignancy</td>
</tr>
<tr>
<td>&gt; 10 ng/mL</td>
<td>Highly suspicious</td>
</tr>
</tbody>
</table>

Prostate cancer is not the only condition that is typically associated with an increased PSA level. Prostatitis, benign prostatic hyperplasia (noncancerous prostate enlargement), ejaculation within 24 hours to 48 hours before testing, and prostatic manipulation (such as with a prostate biopsy) may also elevate PSA levels.\(^3\) The higher the PSA level in the blood, the more likely that cancer is present.\(^7\) PSA testing over time
is also used in some clinical trials to monitor the response to therapy.

Benign prostatic hyperplasia, a condition that arises in most older men, shares some of the symptoms of prostate cancer. Symptoms of benign prostatic hyperplasia can be characterized as obstructive, reflecting encroachment by the enlarged prostate on the urethra. The American Urological Association has developed a symptom index that may be used to classify the severity of the symptoms.\textsuperscript{9} Physicians rely on the results of DRE, PSA testing, and imaging procedures to distinguish between benign prostatic enlargement and prostate cancer. A biopsy provides the convincing evidence that indicates that a malignancy is present.\textsuperscript{10}

In attempts to further refine PSA testing and make it a more useful screening and diagnostic tool, researchers are exploring variations on the standard PSA test. These include:\textsuperscript{7}

- \textit{Percent free-PSA ratio} - assesses the proportion of free and protein-bound PSA; the test was recently approved by the Food & Drug Administration
- \textit{PSA density} - expresses the PSA value in terms of the prostate volume; a prostate-specific antigen density $< 0.15$ is considered normal
- \textit{Age-specific PSA referencing} - uses normal and abnormal values that are specific for different age groups
- \textit{PSA velocity} - examines how quickly (or if at all) the PSA value increases over time; a PSA increase of $> 0.75$ ng/mL per year requires further work-up
Transrectal Ultrasound (TRUS). In this procedure, an ultrasound probe is inserted into the rectum and the prostate is visualized. TRUS is also used during a prostate biopsy to locate the proper area to obtain a tissue sample.  

Screening Recommendations

The American Cancer Society recommends that an annual PSA and DRE be offered to all men aged 50 and older as part of a yearly examination. For men who are at higher risk, however, such as African-Americans and those with a strong family history, screening should begin by age 40. But prostate cancer screening is not without controversy. Not all clinicians or oncology-related groups subscribe to the belief that routine screening should be actively promoted, chiefly because there is no clear-cut evidence that screening reduces mortality from prostate cancer, and we are uncertain that all cancers detected will be of clinical importance in the years to come.

Review Points

- Diagnostic tools for prostate cancer include DRE, PSA testing, a history and physical examination, and a transrectal ultrasound and biopsy
- The higher the PSA value the greater the cancer risk
- All men 50 years and older should have a yearly PSA test, a DRE, and a history and physical examination
- Men with risk factors for prostate cancer should begin screening by age 40
Tumor staging is carried out for two important reasons: to help establish prognosis and to direct therapy. Current therapeutic guidelines are based on the stage of the prostate cancer at the time of diagnosis.

Several different staging systems have been used over the years to assess cancer of all types. No staging system is embraced by all, but the one that has the most widespread acceptance, and is part of the NCCN guidelines, is the *TNM Staging System*. The TNM Staging System can be used for virtually any solid tumor type.

- **T** = Primary tumor
- **N** = Regional lymph nodes
- **M** = Distant metastasis
TNM Staging System for Prostate Cancer

Primary tumor (T)

TX  Primary tumor cannot be assessed

T0  No evidence of primary tumor

T1  Clinically unapparent tumor not palpable or visible by imaging

T1a  Tumor incidental histologic finding in 5% or less of tissue resected

T1b  Tumor incidental histologic finding in more than 5% of tissue resected

T1c  Tumor identified by needle biopsy (eg, because of elevated PSA)

T2  Tumor confined within the prostate

T2a  Tumor involves one lobe of the prostate

T2b  Tumor involves both lobes of the prostate

T3  Tumor extends through the prostatic capsule

T3a  Extracapsular extension (unilateral or bilateral)

T3b  Tumor invades the seminal vesicle(s)
T4    Tumor is fixed or invades the adjacent structures other than seminal vesicles: bladder neck, external sphincter, rectum, levator muscles, and/or pelvic wall

Regional Lymph Nodes (N)

NX    Regional lymph nodes cannot be assessed
N0    No regional lymph node metastasis
N1    Metastasis in regional lymph node

Distant Metastasis (M)

MX    Presence of distant metastasis cannot be assessed
M0    No distant metastasis
M1    Distant metastasis
      M1a Nonregional lymph node(s)
      M1b Bones(s)
      M1c Other site(s)

Staging of Metastatic Disease (modified TNM)

D0    Organ confined, elevated prostatic acid phosphatase
D1    Positive lymph nodes all below aortic bifurcation
D2    Positive lymph nodes above aortic bifurcation; bony metastasis
D3    Distant metastases
Work-Up After Initial Diagnosis

After prostate cancer has been initially diagnosed, NCCN Practice Guidelines recommend that prior to a staging work-up, patients are assessed for life expectancy and symptomatology. If a patient is asymptomatic and is expected to live less than five years, the NCCN Guidelines suggest that a further staging work-up be avoided.10

For patients in whom life expectancy is five years or greater, or who are symptomatic, further evaluation is warranted. The objective of the staging work-up is to determine the full extent of metastasis. All patients should have a complete blood count, serum creatinine, and alkaline phosphatase. Patients who are classified as T1 or T2, and who have a PSA > 10 ng/mL or a Gleason score ≥ 8, should have a bone scan. All patients who are classified as T3 or T4 and all patients who are symptomatic should also have a bone scan. Patients with a grade T3 or T4 who have bulky primary tumors should also have computed tomography (CT) or magnetic resonance imaging (MRI) to evaluate the pelvic lymph nodes. Fine needle aspiration may be performed on enlarged lymph nodes.10
Review Points

_ Staging is carried out to help establish the prognosis and to direct therapy

_ The three components of prostate cancer staging are the primary tumor size and degree of invasion of surrounding tissues, the involvement of regional lymph nodes, and distant metastasis; also important is the pre-treatment PSA value
Although the primary care physician often arrives at the initial diagnosis of prostate cancer, therapeutic management is generally within the purview of a urologist. Medical oncologists have historically not been involved in the care of the patient, unless or until the disease progresses and salvage or palliative therapy is necessary. Now, though, it is becoming more common for medical oncologists to participate in the care of the patient earlier in the disease course.

This section will provide an overview of the therapeutic interventions available to clinicians. It will then review the care of patients at different stages of prostate cancer.

**Therapeutic Modalities**

**Surgery.** The first prostate cancer surgery dates to the late 1800s.³ Surgical management of patients with prostate cancer consists of two major options, and a third which is less commonly employed.

The first surgical option is *radical prostatectomy*. In this procedure, the surgeon removes the entire prostate gland (hence the word ‘radical’ meaning entire, and ‘ectomy’ refers to removal) and some of the surrounding tissue. Radical prostatectomy is performed when the cancer is thought to be localized to the prostate gland itself. There are two types of radical prostatectomy: *radical retropubic prostatectomy* and
radical perineal prostatectomy. They differ in the placement of the incision. In a radical retropubic prostatectomy, the surgeon makes an incision in the lower abdomen. The surgeon can also remove lymph nodes during this procedure, and can make use of a nerve-sparing technique in which nerves on both sides of the prostate gland are not severed or removed. Leaving these nerves intact reduces but does not eliminate the likelihood that the patient will be impotent (unable to have an erection) or incontinent (unable to control the bladder) following surgery. In a radical perineal prostatectomy, the surgeon makes an incision between the scrotum and the anus (the perineum) and removes the prostate gland through this opening. There is no nerve-sparing option with a perineal prostatectomy, and therefore patients will probably experience incontinence and impotence to some degree following the surgery. Lymph nodes cannot be removed during this operation, but they could be removed later through laparoscopic surgery.14

The second surgical option is transurethral resection of the prostate (TURP). In this procedure, only the part of the prostate gland that surrounds the urethra is removed. TURP is reserved for patients who, because of ill health or advanced age, cannot have a radical prostatectomy, and for patients with obstructive symptoms. Rather than a curative procedure, TURP is a palliative one, in that it can reduce the symptoms of prostate cancer or benign enlargement. TURP is more often used for benign prostatic hyperplasia, a noncancerous enlargement of the prostate. In TURP, no incision is made; rather, a wire is inserted up the urethra to the prostate gland, and electrical current is used to cut the tissue.11
Cryosurgery is the third type of surgery that can be used. Through a perineal incision, a probe that is cooled by liquid nitrogen is inserted into the affected area of the prostate gland and freezes the tissue, killing it. At this time cryosurgery is considered less successful than more traditional surgical methods, and is reserved for men who cannot have surgery or radiation therapy.¹¹

Radiation therapy. With radiation therapy, high-energy rays and particles (electrons, protons, photons) are used to kill the cancer cells. Radiation therapy may be used when the cancer is limited to the prostate gland (T1, T2; localized) or has spread to adjacent tissue (T3; locally advanced). In patients in whom the tumor has metastasized, radiation therapy is used to reduce the tumor bulk and for palliation of pain. The two major types of radiation therapies are external beam radiation and brachytherapy.¹¹

External beam radiation is a type of x-ray therapy where the x-rays originating outside the body are directed at the cancerous region. Courses of therapy may last for several weeks. There are two new types of external beam radiation that appear to reduce side effects and increase the efficacy of the treatment. Three-dimensional conformal radiation therapy uses computers to map out exactly the location of the prostate cells; the patient wears a body mold so the x-ray beam can be precisely aimed. The beam “conforms” to the gland, minimizing the scatter of radiation to normal structures such as the bowel and bladder. The second new type is conformal proton beam radiation therapy, which is similar to the three-dimensional conformal radiation therapy except protons are used instead of x-rays. Protons can travel through unaffected tissues and
organs but kill the cancer cells at which they are directed.11

*Brachytherapy*. With brachytherapy, also known as *internal beam radiation therapy*, seed implants, or interstitial implants, radioactive pellets are implanted within the cancerous region. The pellets are radioactive for a certain period of time, generally weeks or months. In high-dose brachytherapy, a needle containing radioactive material is placed within the cancerous region for a day or less and then removed.11

To reduce bone pain that may occur with metastatic prostate cancer, strontium 89 may be injected intravenously. This radioactive analog of calcium has an affinity for bone that is harboring cancer cells, and can kill those cancer cells.11

*Hormone Therapy*. With hormonal therapy, the goal is to ablate the production of androgens, the male sex hormones. The predominant androgen is testosterone, which is produced primarily within the testicles. Hormonal therapy is thought to work best when it is begun soon after prostate cancer has advanced. It is used mainly in patients with advanced prostate cancer, but it is not a cure. Investigators are also researching the use of adjuvant (after radiation or surgery) and neoadjuvant (before radiation or surgery) hormonal therapy.11

Researchers have theorized that there are three different types of prostate cancer cells: androgen-dependent, androgen-sensitive, and androgen-independent cells. Within a single patient, one, two, or all three types of cells may be growing. Androgen-dependent
prostate cancer cells require androgens to grow and divide, and without the presence of androgens, these cells will die. Androgen-sensitive cancer cells grow more rapidly in the presence of androgens, but they do not die if no androgen is present. Androgen-independent prostate cancer cells are oblivious to androgens, and grow and divide without regard to their presence. Clearly, hormonal therapy does not kill all types of prostate cancer cells.³

An alternative hormonal approach is being investigated. Intermittent hormonal therapy, in which patients receive cyclic doses of hormones, alternating with rest periods of no hormones, may help patients better tolerate the side effects of hormonal therapy.³

There are several different types of hormone therapy:

✔ Orchiectomy - surgical removal of the testicles (castration); obviously this is an irreversible treatment

✔ Luteinizing hormone-releasing hormone (LHRH) analogs - these drugs, which include leuprolide (Lupron®) and goserelin (Zoladex®), function at the level of the pituitary gland in the brain to shut down the signal to the testes to produce testosterone

✔ Anti-androgen therapy - to achieve total androgen blockade, these drugs are used in combination with orchiectomy or LHRH analogs; they block the production of androgens by the testes; drugs of this type are flutamide (Eulexin®), bicalutamide (Casodex®), and nilutamide (Nilandron®). Others, such as ketoconazole (Nizoral®) work at the level of the adrenal gland.
✓ Other hormonal agents - usually used after first-line hormonal therapy has failed, these drugs include diethylstilbestrol (DES), megestrol acetate (Megace®), and medroxyprogesterone (Provera®)

Chemotherapy. Historically, chemotherapy has been reserved for patients with prostate cancer who have advanced disease. (Chemotherapy is being evaluated earlier in the disease course in some new protocols.) The NCCN practice guidelines recommend two sequential courses of one of the following regimens:¹⁰

✓ paclitaxel (TAXOL®) + estramustine (Emcyt®)

✓ ketoconazole (Nizoral®) + doxorubicin

✓ estramustine + vinblastine (Velban®)

✓ etoposide (VEPESID®) + estramustine

✓ mitoxantrone (Novantrone®) + prednisone

Expectant monitoring (watch and wait, watchful waiting, deferred therapy). For a select group of patients diagnosed with prostate cancer, a physician may initially recommend no therapeutic intervention. Expectant monitoring may be indicated when prostate cancer is at a very early stage, or when patients are of an advanced age or have a shortened life expectancy. Prostate cancer often spreads very slowly in older men. But expectant monitoring doesn’t mean that the physician does nothing. During a period of deferred therapy, patients receive periodic PSA tests, DRE, and transrectal ultrasound-
guided biopsies. At some point, patients in whom expectant therapy was initially recommended may require other therapeutic modalities.11

Management of Patients with Prostate Cancer

The NCCN practice guidelines for prostate cancer, shown on page [[insert]], recommend management based on several criteria, which will be reviewed here.

Initial therapy. For newly diagnosed patients with prostate cancer who are asymptomatic and whose life expectancy is less than 5 years, no staging work-up is recommended unless and until symptoms surface. For many of these patients, expectant monitoring may be indicated. Similarly, patients with clinical stage T1a can also receive expectant therapy. If, however, patients with clinical stage T1a have a life expectancy beyond ten years, or have a Gleason score greater than 7 or a PSA post-TURP greater than 10, radiotherapy or radical prostatectomy may be considered. The rationale for more aggressive therapy for the latter group is the combination of a minimal tumor size and indicators that the disease is likely to metastasize.10

For patients with T1b, T1c, or T2 disease, therapy is directed by the clinician’s assessment of metastatic potential. Patients with high Gleason scores and PSA values are more likely to experience metastasis. A secondary consideration is the patient’s life expectancy. Once all of these factors are taken into account, expectant therapy, radiotherapy, or radical prostatectomy may be recommended, with more aggressive
therapy reserved for patients with a higher risk of metastatic disease and a longer life expectancy. The therapeutic goal of patients in this category is a cure.\textsuperscript{10}

Initial therapy for patients with T3a disease is less clear-cut, since there is no consensus regarding whether all such patients are potentially curable (and therefore aggressive therapy is still warranted) or whether in some patients there is little reasonable chance for a cure (suggesting that expectant therapy is more appropriate). Experts suggest that if the tumor is still fairly small and the Gleason score is less than 7, radical prostatectomy may be an option. For most other patients, though, androgen ablation or radiotherapy or a combination of the two may be the most appropriate option.\textsuperscript{10}

In patients with advanced disease (T3b, T3c, T4N0), initial therapy may consist of androgen ablation or radiotherapy or a combination of the two. For patients in this group with positive lymph nodes and/or distant metastasis, palliation is the goal of therapy, not cure. Androgen ablation is the recommended initial course of therapy.\textsuperscript{10}

**Progressive disease.** Salvage therapy in patients with progressive disease may be either radiotherapy or androgen ablation. For palliative therapy in patients with androgen-independent tumors, combination chemotherapy, supportive care with prednisone, or local radiotherapy may be used.
Chemoprevention of Prostate Cancer

Researchers are exploring ways to prevent prostate cancer. As mentioned earlier, preliminary reports suggest that lycopene and selenium may have a positive effect, but no conclusive evidence of that is available. Another study found that long-term use of a vitamin E supplement reduced prostate cancer incidence and deaths among smokers.\textsuperscript{15} Enrollment is underway for a placebo-controlled clinical trial in 18,000 men over 55 years old to establish whether finasteride (Proscar\textregistered) reduces the incidence of prostate cancer.\textsuperscript{16}

Patient Education

To assist patients in learning about prostate cancer, pharmacists may wish to consult \textit{Prostate Cancer: Treatment Guidelines for Patients},\textsuperscript{17} produced jointly by the American Cancer Society and the NCCN. The American Cancer Society has additional patient education materials available at their web site, http://www.cancer.org.

Future Directions

Research into the optimal management of prostate cancer continues. Use of vaccines, which can modulate the immune response to a malignancy, is being explored.\textsuperscript{3} PSA monitoring is allowing investigators to re-examine the recognized standard therapies for prostate cancer. Antiangiogenesis agents are also being tested.\textsuperscript{3} Since patients are diagnosed earlier in the course of the disease, and high-risk patients are receiving treatment even before the onset of symptoms, there may be an increased response to
therapy.³ Use of chemotherapeutic agents earlier in the disease course is also being explored, as is the neoadjuvant role and chemotherapy-hormonal combinations.

Review Points

- Surgical options for the management of prostate cancer include radical prostatectomy, transurethral resection of the prostate, and cryosurgery.
- External beam radiation and internal beam radiation therapy are the two main methods of delivering radiation to the tumor site.
- Hormonal therapy for prostate cancer involves the reversible or irreversible blocking of androgen production, chiefly the male hormone testosterone, which is produced by the testes.
- Therapy for prostate cancer is dependent on several factors, including the life expectancy of the patient, the stage at initial diagnosis, and the risk of metastasis.
CONCLUSION

Despite advances in its diagnosis and treatment, prostate cancer still claims many lives each year. Yet, these advances are enabling clinicians to identify patients at high risk of recurrence, and to treat these patients more aggressively. As regular screening for prostate cancer in men over 50 years with a PSA test and a DRE (and screening earlier in high-risk patients) becomes a more common practice, the hope is that more cases of prostate cancer will be found earlier in the disease course, and aggressive management can be accomplished in patients at high risk for metastasis.

Management of prostate cancer is based on a combination of four options: surgery, radiation therapy, hormonal therapy, and chemotherapy. Novel approaches and combinations may yield better results, and research is needed to pursue innovative treatment strategies, and to challenge the so-called standard therapies. A multidisciplinary partnership involving the primary care physician, the urologist, the medical oncologist, the pharmacist, and support personnel is most likely to be of benefit to patients.
REFERENCES


Post-Program Self-Assessment

Directions: Circle the single most appropriate response to the questions or incomplete statements below. To receive ACPE credit, you must also record your responses on the reply form on page XX. Seventy percent or more correct responses are required to earn continuing education credit. A certificate will be returned for your records.

1. A man’s lifetime risk of developing prostate cancer is ____________.
   a. 1 in 9
   b. 1 in 2
   c. 2 in 9
   d. 1 in 6
   e. 1 in 10,000.

2. The most important risk factor for prostate cancer is ______________:
   a. age
   b. race/ethnicity
   c. diet
   d. hormonal factors
   e. all of the above are equally important risk factors.
3. African-Americans are at higher risk of prostate cancer than are whites.
   a. True
   b. False

4. Which of the following **DOES NOT** increase one’s risk of prostate cancer?
   a. one or more first-degree relatives with prostate cancer
   b. a diet high in saturated fat
   c. African-American race
   d. a vasectomy
   e. all of the above factors increase one’s risk of prostate cancer

5. Which of the following is a **true** statement?
   a. Lung cancer is the most commonly diagnosed cancer in men.
   b. When prostate cancer is diagnosed at an earlier stage, the odds of survival are improved.
   c. Histologic prostate cancer is found in 100% of men over the age of 60 years.
   d. American men have a 1 in 6 lifetime risk of developing cancer of any kind.
   e. If two or more first-degree relatives have been diagnosed with prostate cancer, a man’s prostate-cancer risk doubles.
6. The most common type of prostate cancer is___________.
   a. ductal carcinoma
   b. mucinous carcinoma
   c. adenocarcinoma
   d. transitional carcinoma
   e. lobular carcinoma

7. A tumor that has been assigned a Gleason score of 9, and which is poorly differentiated, has a ______ risk of metastasis.
   a. 10%
   b. 20%
   c. 100%
   d. 50%
   e. 75%

8. Signs and symptoms of prostate cancer include:
   a. hematuria
   b. painful ejaculation
   c. urinary frequency and urgency
   d. urinary incontinence
   e. All of the above are associated with prostate cancer.
9. A normal PSA blood test is considered to be__________.
   a. < 4 ng/mL
   b. 6 ng/mL
   c. 8 ng/mL
   d. 4 to 8 ng/mL
   e. < 10 ng/mL

10. Elevated PSA levels may occur with__________________.
    a. prostate cancer
    b. lung cancer
    c. benign prostatic hyperplasia
    d. a and c are correct answers.
    e. a, b, and c are correct answers.

11. The American Cancer Society recommends a yearly PSA determination and DRE in all men__________________.
    a. over 65 years of age
    b. under 50 years of age
    c. over 65 years of age
    d. 50 years of age and older
    e. with colorectal cancer
12. The TNM Staging System assesses the primary tumor, the regional lymph nodes, and the presence of distant metastasis.
   
   a. True
   
   b. False

13. ________________is used to reduce the bone pain that may occur with prostate cancer.
   
   a. Cryosurgery
   
   b. Strontium 89
   
   c. Internal beam radiation
   
   d. Transurethral resection of the prostate

14. Expectant therapy may be appropriate for patients who ________________.
   
   a. have a life expectancy of 10 years or greater and who have a Gleason score of 8
   
   b. are symptomatic and have a life expectancy greater than 10 years
   
   c. have high Gleason scores and are symptomatic
   
   d. are older, or who have a shorter life expectancy
   
   e. have T2 disease and have high Gleason scores
15. The goal of hormonal therapy in prostate cancer is to_____________________.

   a. render the patient sterile
   b. block the production of cortisol
   c. reduce the production of testosterone
   d. obliterate the androgen-independent prostate-cancer cells
   e. help patients better tolerate the side effects of chemotherapy