

## Prostate Cancer

## Yesterday

- In the mid 1970s, the annual death rate from prostate cancer in the United States was approximately 31 per 100,000 men, with African American men having a higher rate of approximately 55 per 100,000 men compared to white men with a rate of about 29 per 100,000 men.
- During the period 1974-1976, the 5-year overall survival rate for men diagnosed with prostate cancer was 69 percent. Among white men, the 5-year overall survival rate was 70 percent; among African American men, it was 61 percent. These survival rates may have been influenced by the method used to initially diagnose prostate cancer in the 1970s, i.e., digital rectal examination (DRE), which uses palpation to detect tumors. Tumors detected by DRE are often advanced.
- Early treatment options for prostate cancer included surgery, radiation therapy, and hormonal therapy (i.e., reducing male hormone levels either by removing the testicles or by administering estrogens, including diethylstilbestrol [DES]). Prostate cancers initially require male hormones, such as testosterone, to grow. Therefore, prostate tumors can often be treated by methods that lower blood levels of these hormones.
- In 1974, the National Cancer Institute (NCI) established the National Prostatic Cancer Project, an initiative that enabled collaborations among cancer researchers, epidemiologists, and pathologists to plan, coordinate, direct, and monitor the research being pursued in prostate cancer.
- African American men have mortality rates that are more than twice the rates observed in other racial and ethnic groups in the United States. An ongoing NCI-supported study is investigating a variety of risk factors that may contribute to the higher incidence and mortality rates observed in African American men.
- In the late 1980s, the widespread adoption of the prostate-specific antigen (PSA) test represented a major improvement in the management of prostate cancer. This test measures the amount of PSA protein in the blood, which is often elevated in patients with prostate cancer. In 1986, the U.S. Food and Drug Administration approved the use of the PSA test to monitor patients with prostate cancer and, in 1994, additionally approved its use as a screening test for this disease.
- Due to the widespread implementation of PSA testing in the United States, approximately 90 percent of all prostate cancers are currently diagnosed at an early stage, and, consequently, men are surviving longer after diagnosis. However, the results of two ongoing clinical trials, the NCI-sponsored Prostate, Lung, Colorectal, and Ovarian (PLCO) screening trial and the European Study of Screening for Prostate Cancer (ERSPC) will be needed to determine whether PSA screening actually saves lives.
- Advances in the treatment of prostate cancer have included new surgical approaches and improvements in radiotherapy. For example, in 1986, surgeons developed a technique that allowed the removal of the prostate while minimizing nerve damage, thereby decreasing adverse side effects. In addition, clinical researchers improved a long-established radiotherapy technique known as brachytherapy, which involves the implantation of a small amount of radioactive material (seeds) into the prostate. This radiation therapy method is an effective treatment for early-stage prostate cancer.

## Today

- In 2007, an estimated 220,000 men will be newly diagnosed with prostate cancer in the United States and about 28,000 men will die from the disease.
- The most recent report available on cancer mortality shows that, in 2004, the overall death rate from prostate cancer among American men was 25 per 100,000. Since 1994, this rate has decreased by four percent each year, and, in 2004, there were an estimated 2 million prostate cancer survivors in the United States.
- Advances in hormonal therapy for prostate cancer have included the development of gonadotropin-releasing hormone (GnRH) agonists, which inhibit the pituitary gland's ability to stimulate the testes to make testosterone. In 1984, results of a clinical trial showed that the GnRH agonist

leuprolide was equivalent to DES in reducing blood levels of testosterone but caused less cardiovascular toxicity. Other GnRH agonists used today include goserelin, triptorelin, and histrelin.

- Advances have also been made in chemotherapy for prostate cancer. In 2004, results from two large NCI-sponsored clinical trials showed that use of the drug docetaxel could prolong the survival of men who had advanced prostate cancer that no longer responded to hormonal therapy.
- Ongoing clinical trials supported by NCI over the past 25 years have investigated the effectiveness of natural and synthetic compounds in the prevention of prostate cancer. The Prostate Cancer Prevention Trial (PCPT), which enrolled nearly 19,000 healthy men, found that finasteride, a drug approved for the treatment of benign prostatic hyperplasia (BPH), which is a noncancerous enlargement of the prostate, reduced the risk of developing prostate cancer by 25 percent. This was the first study to demonstrate that a drug could be used to prevent prostate cancer. Another trial, the Selenium and Vitamin E Cancer Prevention Trial (SELECT), is studying more than 35,000 men to determine whether daily supplements of selenium and vitamin E can reduce the incidence of prostate cancer in healthy men. Other prostate cancer prevention trials are currently evaluating the protective potential of multivitamins, vitamins C and D, soy, green tea, and lycopene, which is a natural compound found in tomatoes.
- NCI's commitment to basic research has led to recent discoveries that are shedding light on the molecular origins of prostate cancer. One study, reported in 2005, showed that specific genes were fused in 60 to 80 percent of the prostate tumors analyzed. This study represents the first observation of non-random gene rearrangements in prostate cancer. This genetic alteration may eventually be used as a biomarker to aid in the diagnosis and, possibly, treatment of this disease. Other studies have shown that genetic variations in a specific region of chromosome 8 can increase a man's risk of developing prostate cancer. These genetic variations account for approximately 25 percent of the prostate cancers that occur in white men. They are the first validated genetic variants that increase the risk of developing prostate cancer and may help scientists better understand the genetic causes of this disease.
- NCI is also supporting research that examines how proteins circulating in a patient's blood can be used to improve the diagnosis of prostate and other cancers. In 2005, NCI-supported scientists identified a group of specific proteins that reproduced by a patient's immune system in response to prostate tumors. These proteins, a type of autoantibody, were able to detect the presence of prostate cancer cells in blood specimens with greater than 90 percent accuracy. When used in combination with PSA, these and other blood proteins may eventually be used to reduce the

number of false-positive results obtained with PSA testing alone and, therefore, reduce the large number of unnecessary prostate biopsies that are performed each year due to false-positive PSA test results.

## Tomorrow

- NCI is committed to supporting research into the biological and molecular mechanisms of prostate cancer. Programs such as the Institute's Early Detection Research Network (EDRN) and the Clinical Proteomic Technologies Initiative (CPTI) are supporting research to identify biomarkers – substances in blood and tissues – to aid not only in diagnosis but also in prognosis, which is critical in helping men decide whether to undergo immediate therapy (surgery or radiation) or to be observed by their physician (also known as watchful waiting or active surveillance). Furthermore, an NCI initiative is supporting a partnership of scientists who are studying the use of nanoparticles to improve our ability to image (visualize) prostate tumors. These new technologies could lead to more precise targeting of therapies.
- To support investigations into the molecular mechanisms of prostate cancer initiation and progression, NCI has established a collection of high-quality blood and tissue specimens from prostate cancer patients, called a biorepository, which can be used to evaluate genes and proteins as potential clinical biomarkers or targets for drug development.
- Advances are also being made in the development of new surgical techniques, such as robotic-assisted laparoscopic surgery, which may help decrease the time needed to recover from surgery and shorten the length of hospitalization.
- Ongoing NCI-supported clinical trials are evaluating new treatments for prostate cancer. These include studies of molecularly-targeted agents, novel drug combinations, and vaccines designed to help a patient's own immune system fight this disease.