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Key Inforbits

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- Screening and Staging of Prostate Cancer
- 5α-Reductase Inhibitors use in Prostate Cancer
- Ways to Decrease Risk of Prostate Cancer
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- The Last Dose

Prostate Health Month: National Prostate Cancer Coalition
www.menshealthnetwork.org

Prostate Cancer Prevention Awareness

Introduction to Prostate Cancer

Prostate cancer is characterized as a malignant neoplasm that occurs in the prostate gland.[1] The prostate gland produces seminal fluid that, during orgasm, helps carry sperm out of the male's body as part of semen.[1] It is estimated that nearly 30,000 men will die from prostate cancer in 2013, and almost 250,000 new cases of prostate cancer will be diagnosed.[2]

The prostate is composed of acinar secretory cells, which normally secrete digestive enzymes into the gut that are altered when invaded by cancer[1]. Adenocarcinoma is the major pathologic cell type in greater than 95% of prostate cancer cases.[1] Prostate cancer can be classified into four stages (Stage I-IV), ranging from early stage cancer to advanced cancer that has spread to the rest of the body.[2] Well-differentiated tumors grow slowly, where poorly differentiated tumors grow more rapidly and have a poorer prognosis.[1]

Growths in the prostate can be benign or malignant.[2] Benign growths are rarely a threat to life and they don't invade surrounding tissues .[2] Benign growths are also characterized by not spreading to other parts of the body, and generally can be removed and are at a low risk of returning.[2] Malignant growths are threatening to life, and often invade other nearby tissues and organs.[2] Removal of these growths is often not successful at preventing their regrowth.[2] If prostate cancer cells becomes metastatic, the cancer may attach to other tissue to form new tumors that can be damaging.[2]

1. Norris L, Kolesar J. Prostate Cancer. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BR, Posey LM, editors. Pharmacotherapy: A pathophysiologic approach. 8th ed. New York: McGraw-Hill Medical; c2011. p. 2319-2332.
2. What You Need to Know About: Prostate Cancer [Internet]. Rockville, Maryland: National Cancer Institute; c2012. 2012 September 26 [cited 2013 August 19]; [about 10 screens]. Available from: http://www.cancer.gov/cancertopics/wyntk/prostate

Screening and Staging of Prostate Cancer

Current screening approaches for prostate cancer involves offering a baseline prostate specific antigen (PSA) and digital rectal exam (DRE) at age 40 with annual evaluations beginning at age 50 for men with normal risk.[1] Earlier testing is recommended for men with higher risk for prostate cancer (family history, African American, US resident, high fat diet).[1]

DRE is the most commonly used screening for prostate cancer.[1] It has the advantages of specificity, low cost, safety, and ease of performance. DRE can be highly subjective based on the physician administering the procedure.[1] PSA is a glycoprotein produced and secreted by the epithelial cells of the prostate.[1] PSA can be influenced by acute urinary retention, acute prostatitis, and benign prostate hyperplasia (BNP) which limits the usefulness of the test, because of its lack of specificity.[1] PSA is a useful marker for monitoring response to therapy.[1]

Gleason Score

The most commonly used system for grading prostate cancer is the Gleason score.[2] Scores range from 2 to 10.[2]

To determine a Gleason score pathologists look at the pattern of prostate cells taken from a biopsy.[2]

The most common pattern of cells is given a 1 (normal) to 5 (abnormal).[2] A pathologist then adds up the score of the two most common types of cell present, and a score between 2 and 10 is obtained.[2]

Prostate Cancer Staging[2]

Stage 1	Cancer is only in the prostate. Gleason score is 6 or less.
Stage 2	Tumor is more advanced than in stage 1, but the tumor does not extend beyond the prostate.
Stage 3	Tumor extends beyond the prostate. The tumor may invade seminal vesicle, but not lymph nodes.
Stage 4	The tumor may have spread to the bladder, rectum, lymph nodes, bones, or other parts of the body.

5α reductase Inhibitors and their use in Prostate Cancer Prevention

The medications finasteride (Proscar®) and dutasteride (Avodart®) work by competitively inhibiting the enzyme 5α reductase resulting in the inhibition of the conversion of testosterone to dihydrotestosterone (DHT), which is a steroid responsible for prostate growth and possibly plays an important role in prostate cancer.[1,2] Dutasteride is non-selective in its action against 5α reductase. This property causes dutasteride to act more quickly and may reduce serum DHT levels up to 90%, but there appears to be no pharmacodynamic advantage of dutasteride over finasteride. Because of their mechanism of action, 5α reductase inhibitors are the preferred medications for patients with enlarged prostate glands and decrease gland size by up to 25%.[3]

The Prostate Cancer Prevention Trial compares the use of finasteride vs placebo in reducing the occurrence of prostate cancer. In this trial finasteride reduced the incidence of cancer by 25% but showed that the observed cancers were more aggressive. This data was then re-examined and it was thought that the increased aggressiveness of the prostate cancers were due to bias and not an adverse event from finasteride therapy. Initial reports from an additional trial propose that the effects of dutasteride and finasteride are comparable. Using this data, the American Society of Clinical Oncology and the American Urological Association developed a cooperative practice guideline for prostate cancer prevention. In these guidelines it is suggested that patients who are currently symptom free with a PSA level of ≤3.0 ng/mL may potentially benefit from a seven-

year trial of either dutasteride or finasteride but they do not recommend their use due to their suggested higher risk of aggressive type prostate cancer.[4]

1. Finasteride, dutasteride. Lexicomp Online. [AUSHOP Intranet] Hudson, OH: Lexicomp/Wolters Kluwer Health c2013 [updated 2013 August 19; cited 2013 August 19]. [about 2 p.]. Available from: http://online.lexi.com/lco/action/home
2. Prostate Cancer Prevention [website on the internet] Bethesda, MD: National Cancer Institute [updated 2012 May 25; cited 2013 August 19]. Available from: http://www.cancer.gov/cancertopics/pdq/prevention/prostate/Patient/page3
3. Lee M. Benign Prostatic Hyperplasia. In: DiPiro JT, Talbert RL, Yee JC, Matzke GR, Wells BG, Posey LM, editors. Pharmacotherapy: A Pathophysiological Approach. 8th edition. New York: McGraw-Hill Medical; c2011. p. 1455-1466.
   Norris LB, Kolesar JM. Prostate Cancer. In: DiPiro JT, Talbert RL, Yee JC, Matzke GR, Wells BG, Posey LM, editors. Pharmacotherapy: A Pathophysiological Approach. 8th edition. New York: McGraw-Hill Medical; c2011. p. 2319-2332.

Simple Ways to Decrease Your Risk of Developing Prostate Cancer

There are many ways to aid in the prevention of prostate cancer. Some may be as simple as avoiding certain risk factors (eg, smoking and unhealthy foods) and in other circumstances medications may be warranted.

Risk factors attributing to the development of prostate cancer:

Risk Factor	Rationale
Age	Higher incidence of developing prostate cancer is seen in patients > 50 years old.
Family History	Incidence is typically higher in patients with a first degree relative that has previously had the disease
Race	More often seen in African-Americans than seen in Caucasians.
Increased dihydrotestosterone (DHT) levels	DHT is responsible for normal prostate growth. If levels are elevated the incidence of prostate cancer is increased.
Vitamin E	When taken alone
Folic acid	Normal levels obtained by a balanced diet is protective, increased intake of 1 mg folic acid has increased risk of developing prostate cancer.

While some of these risk factors are unavoidable (eg, age, family history, race) others can be avoided. These steps can be taken to help avoid developing cancer:

• Life style changes
• Avoidance of modifiable risk factors
• The use of medications that treat conditions that precede cancer.[1]

1. Prostate Cancer Prevention [website on the internet] Bethesda, MD: National Cancer Institute [updated 2012 May 25; cited 2013 August 19]. Available from: http://www.cancer.gov/cancertopics/pdq/prevention/prostate/Patient/page3

Recent Developments

In 2003, the Prostate Cancer Prevention Trial established that Proscar® (finasteride) significantly reduced the risk of prostate cancer. Among 18,880 men with prostate cancer, 10.5% of 9423 men treated with finasteride were diagnosed with prostate cancer and 14.9% of 9457 men not treated with finasteride were diagnosed with prostate cancer. There were a total of 1412 men in the finasteride group and 989 men in the placebo group who were diagnosed with prostate cancer. The trial also evaluated the prevalence of high-grade cancer among both groups of men that were diagnosed with prostate cancer. The trial found that men who were treated with finasteride were more likely to develop high-grade cancer (3.5%) versus those who were not

treated with finasteride (3%). This correlation required more research to understand the significance of the difference.[1]

Most recently (August 15, 2013), the *New England Journal of Medicine* published an 18 year follow up comparing the survival rates of prostate cancer patients treated with finasteride to those not treated. The study found there was no significance difference in the rate of developing cancer among either group or survival after diagnosis. The ten-year survival rate for men with high-grade prostate cancer was 73% (finasteride) vs 73.6% (placebo). The ten-year survival rate for men with low-grade prostate cancer was 83% (finasteride) vs 80.9% (placebo). The use of finasteride improved the sensitivity of PSA (prostate specific antigen) testing and therefore dramatically improved the rate of diagnosis. A majority of the increased diagnoses were low-grade cancers (Gleason Score 2-6) that were attributed to the increased sensitivity provided by finasteride.[1]

In conclusion, finasteride has been shown to decrease the risk of prostate cancer by 30%. Even though men taking finasteride are more likely to develop high-grade prostate cancer, there is no significant difference in mortality rates up to 18 years. The ability of finasteride to improve prostate cancer diagnosis, mostly low-grade prostate cancer, may seem groundbreaking; however the authors conclude that over diagnosis of low-grade prostate cancer is greatly problematic. They note that treatment of low-grade cancers has little to no benefit and that treatment causes "considerable burden to the patient and to society."[1]

1. Thompson IM, Goodman PJ, Tangen CM, Parnes HL, Minasian LM, Godley PA, et al. Long-term survival of participants in the prostate cancer prevention trial. N Engl J Med. 2013;369(7):603-610.

Other Important Observances In September

- Alzheimer's Awareness Month
- Cholesterol Education Month
- Pain Awareness Month
- Thyroid Cancer Awareness Month

The last "dose" …

"The quandary in prostate cancer: Is cure necessary in those for whom it is possible, and is cure possible in those for whom it is necessary?"

~ Willet Whitmore, Jr., M.D. [Urologic cancer surgeon, 1917 – 1995)

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