

PROSTATE CANCER

Prostate Anatomy

The prostate is a part of the male reproductive system. It normally is about the size and shape of a walnut and weighs about 18 grams. The prostate is located below the bladder and lies in front of the rectum. A portion of the male urethra passes through the prostate and carries urine from the bladder out through the penis. The main function of the prostate is to produce seminal fluid. Male hormones, also called androgens, are responsible for the growth of the prostate. Testosterone, the predominant androgen, is produced primarily in the testicles with the adrenal glands supplying a small amount.

Risk Factors

Prostate cancer is the most common non-skin cancer diagnosed in men and the second most common cause of cancer related deaths in men. One out of six men will be diagnosed with prostate cancer during their lifetime, with 186,000 new diagnoses and 28,000 deaths expected this year. That equates to one diagnoses every 3 minutes and one death every 18 minutes.

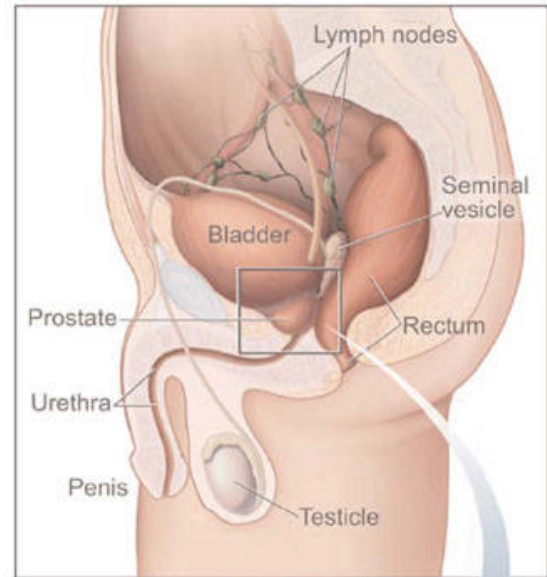
The risk of prostate cancer increases with advancing age; however, 25% of men will be diagnosed under the age of 65, and it is estimated that one-third of 50 year old men have cancerous cells in their prostate. Prostate cancer is twice as common in African American males. Men with 1st and 2nd degree relatives diagnosed with prostate cancer are at a two- threefold increased risk of developing prostate cancer. Many factors including genetics, age and race play a role in the development of prostate cancer. Lifestyle factors that may increase the risk of development of prostate cancer include obesity as well as diets high in saturated fats.

Screening

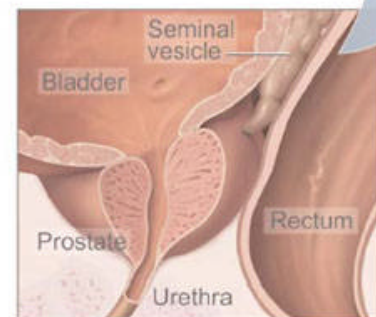
The American Urologic Association recommends that both a prostate-specific antigen (PSA) blood test and digital rectal examination (DRE) be offered annually, beginning at age 45-50, to men who have at least a 10-year life expectancy. Men at high risk (African-American men and men with a strong family history (one or more first-degree relatives diagnosed before age 65) should begin testing at age 40.

What is PSA?

PSA is a protein excreted by the prostate involved in liquefying the semen. A small portion is released into the bloodstream and is easily measured with a blood test. If a higher than normal level is detected,



This shows the prostate and nearby organs.



This shows the inside of the prostate, urethra, rectum, and bladder.

it may represent a prostate infection, prostate inflammation, or prostate enlargement (also known as BPH). An elevated PSA may also be a sign of prostate cancer. Determining what an elevated PSA means may be complicated. While a single PSA value is helpful, having multiple PSA values over time is generally most informative. A free and total PSA may also be added to the routine PSA test. This adjunctive test may provide more information to your doctor about the PSA, if necessary.

Diagnosis

If either the prostate specific antigen (PSA) or the digital rectal exam (DRE) is abnormal, then a prostate biopsy may be indicated. Only a tissue sample from biopsy can accurately detect the presence of prostate cancer. A prostate biopsy is an outpatient procedure which involves placing an ultrasound probe into the rectum so as to visualize the prostate. Guided by images from the probe, your doctor uses a fine, spring-propelled needle to retrieve several very thin sections of tissue from your prostate gland. Prostate cancer cannot be diagnosed by ultrasound imaging alone but is known to exist in the periphery of the prostate gland. As such, while the biopsies are directed to this area, detection of prostate cancer is not 100% and men with a negative biopsy still need to be monitored.

A pathologist will determine if the tissue is cancerous and estimate how aggressive it appears. This information is relayed as a Gleason score. In this system, the pathologist evaluates the biopsy specimen under a microscope, looking for cancerous appearing glands. A grade from 1 to 5 is given, with a lower grade corresponding to a less aggressive pattern and a higher to a more aggressive pattern. The predominant pattern will be given the first number, i.e. 3. The pathologist then looks through the specimen again to see if a smaller volume another pattern is present, and if so, it is given a number based on its pattern, i.e. 4. The total Gleason score would then be a $3+4=7$. If only pattern 3 is seen, then the Gleason score would be $3+3=6$. Scores of 6 and below are considered less aggressive cancers, 7 is intermediate and 8, 9 and 10's are more aggressive. The 7 is split, with a $3+4=7$ behaving more like a 6 while a $4+3=7$ acts more like an 8. Higher grades of prostate cancer are more likely to grow and spread outside of the prostate.

Staging

Once cancer is detected, your physician may recommend a metastatic evaluation. This will be based upon your particular diagnosis, taking into account the Gleason score, the volume of disease detected on the biopsy, the overall PSA and the rate of rise of the PSA. Detection of asymptomatic metastatic disease in prostate cancer is greatly affected by the staging tests performed. Radionuclide bone scans are currently the most widely used tests for detection of metastases to the bone, and CT scans are used to evaluate for soft tissue spread, particularly to pelvic lymph nodes. Although enlarged lymph nodes can occasionally be visualized, because of a stage migration associated with PSA screening, very few patients will be found to have nodal disease, so false-positive and false-negative results are common when imaging tests are employed. In lieu of imaging, risk tables are generally used to determine individual patient risk of nodal involvement. Additional imaging including either a Prostatecint scan and/or an endorectal MRI is utilized if necessary.

The TNM staging system below is the most commonly employed system.

Primary tumor (T)

- TX: Primary tumor cannot be assessed
- T0: No evidence of primary tumor
- T1: Clinically inapparent tumor not palpable nor 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 (e.g., because of elevated PSA)
- T2: Tumor confined within prostate*
- T2a: Tumor involves 50% or less of one lobe

- T2b: Tumor involves more than 50% of one lobe but not both lobes
- T2c: Tumor involves both lobes
- T3: Tumor extends through the prostate capsule**
- T3a: Extracapsular extension (unilateral or bilateral)
- T3b: Tumor invades seminal vesicle(s)
- T4: Tumor is fixed or invades 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 were not assessed
- N0: No regional lymph node metastasis
- N1: Metastasis in regional lymph node(s)

Distant metastasis (M)*

- MX: Distant metastasis cannot be assessed (not evaluated by any modality)
- M0: No distant metastasis
- M1: Distant metastasis
- M1a: Nonregional lymph node(s)
- M1b: Bone(s)
- M1c: Other site(s) with or without bone disease

Treatment

Men with prostate cancer have many treatment options. The treatment that's best for one man may not be best for another. The options include active surveillance (also called watchful waiting) , surgery, radiation therapy, hormone therapy, and chemotherapy. You may have a combination of treatments. The treatment that's right for you depends mainly on your age, Gleason score, the number of biopsy tissue samples that contain cancer cells, the stage of the cancer, your symptoms, and your general health. Your doctor can describe your treatment choices, the expected results of each, and the possible side effects. You and your doctor can work together to develop a treatment plan that meets your specific medical and personal needs.

Watchful Waiting: Watchful waiting is often called "active surveillance" or "observation" and means that you decide to have no active treatment now. Your doctor will want to follow you closely to look for any signs that the disease may be changing. You will have tests like the ones you've already had such as digital rectal exams, PSA tests, and repeat biopsies. You can change your mind and decide to have treatment at any time. Watchful waiting is based on the fact that many early-stage prostate cancers grow so slowly that they may never cause problems or become life threatening.

Medical Management: Hormone therapy involves either inhibiting the production of the male hormone testosterone, a stimulator of prostate cancer cell growth, or blocking its effect at the cell level. Intramuscular injection of medications known as gonadotropin receptor agonists (GnRH agonists) blocks the message from the brain that signals the testicles to make testosterone. Another group of medications known as anti-androgens block the ability of cells to recognize testosterone. These two classes of medications are combined at times based on prostate cancer risk factors. Hormone therapy is utilized in early-stage cancers to shrink large tumors to ease treatment or in combination with radiation therapy to improve curative potential in more aggressive cancers. In men with advanced prostate cancer where cure is not possible through surgery or radiation, this form of treatment is effective in helping to both shrink the cancer and slow its growth. Unfortunately, simply depriving prostate cancer of testosterone does not kill all of the cancer cells. Within a few years, the cancer often learns to thrive without testosterone. Once this happens, hormone therapy is less likely to be effective and the cancer is deemed hormone independent or hormone refractory.

Side effects of hormone therapy can include breast enlargement (gynecomastia), reduced sex drive, erectile dysfunction, hot flashes, weight gain and reduction in muscle and bone mass. Long term side effects may include development of osteoporosis and increased risk of heart disease.

External Beam Radiation Therapy (EBRT or XRT): Focused radiation delivered from a linear accelerator kills cancer in your prostate while minimizing harm to surrounding tissue. Treatments are generally given five days a week for six to eight weeks. Each treatment appointment takes 10-15 minutes— radiation is received for about one minute. Intensity Modulated Radiation Therapy (IMRT), a more precise form of radiation delivery, precisely shapes radiation to fit a tumor. Radiation beams are broken into many smaller “beamlets,” and the intensity of each is adjusted individually. IMRT further reduces the amount of radiation to normal tissues near the tumor. IMRT also may allow a higher dose of radiation to the tumor, increasing the chance of a cure.

Brachytherapy: This is a type of internal radiation therapy. It is also called “seed implants” or low dose rate permanent brachytherapy. Radiation is delivered inside your body by implanting tiny seeds in your prostate. Each seed has a small amount of radioactive material that emits radiation within an inch of its surroundings. Low-dose seeds are left in the prostate permanently, although their radiation lasts for only 3 to 6 months. This procedure is usually done on an outpatient basis without a hospital stay.

High Dose Rate (HDR) Brachytherapy: This is also a type of internal radiation. HDR temporary brachytherapy involves placing very tiny plastic catheters into the prostate gland, and then giving a series of radiation treatments through these catheters. The catheters are then easily pulled out, and no radioactive material is left in the prostate gland. Because the computer can control how long a single seed remains in each of the catheters, the radiation dose in different regions of the prostate is precisely controlled. The tumor receives a higher dose while ensuring that the urine passage (urethra) and rectum will receive a lower dose. This ability to modify the dose after the needles are placed is one of the main advantages of temporary brachytherapy over permanent seed implants. Based upon tumor characteristics and staging, HDR can either be performed as a single therapy or may be combined with a short, low course of external beam radiation therapy.

The most common issues arising from radiation include urinary and rectal irritation as well as sexual side effects. Voiding issues can include urinary urgency, frequency or burning with urination. These are usually temporary, gradually diminishing a few weeks after completing treatment. Bowel effects range from loose stools, rectal bleeding, discomfort during bowel movements or a sense of needing to have a bowel movement (rectal urgency). In some cases these problems persist for months after treatment, but they most often improve on their own. Radiation therapy does not usually cause immediate sexual side effects such as erectile dysfunction, but some men may notice a gradual loss of erectile function over the following years.

Surgery: Surgical removal of the prostate for cancer is called a radical prostatectomy and is often the treatment choice for healthy men who have early-stage prostate cancer. The prostate can be removed via an open surgical approach, either through a lower midline abdominal incision from the umbilicus to the pubic bone (radical retropubic prostatectomy, RRP) or through an incision from the base of the scrotum to the anus (radical perineal prostatectomy, RPP). The newest method of removing the prostate for cancer is robotic radical prostatectomy, a minimally-invasive surgical technique in which the prostate gland is removed with the assistance of a robot that extends the capabilities of the surgeon.

Urinary incontinence and impotence are the most common long term issues arising from surgical removal of the prostate. Incontinence is the inability to control urine and may result in leakage or dribbling of urine, especially just after surgery. Normal control returns for many patients within

several weeks or months after surgery, although some patients may become permanently incontinent. Impotence is the inability to have an erection sufficient for penetration. This is a common side effect after radical prostatectomy. Nerves on both sides of your prostate that control erections may be damaged or removed during surgery. The majority of men under the age of 50 who have nerve-sparing surgery are able to achieve erections afterward, and even some men in their 70s are able to maintain normal sexual functioning. Men who have trouble achieving or maintaining an erection before surgery have a higher risk of being impotent after the surgery.

Alternative Treatments: New methods for treating prostate cancer continue to arise.

- Cryotherapy or cryoablation of the prostate involves the controlled freezing of the prostate gland in order to destroy cancerous cells. This is accomplished by placing multiple small probes into the prostate through the perineum (the area between that scrotum and the rectum). Liquid nitrogen is passed through the probes to create an ice ball that envelops the prostate. The ice ball is monitored via an ultrasound probe placed in the rectum. With improvements in technology, imaging and freezing techniques, PSA undetectability and negative biopsy rates have improved and the risk of complications has been reduced. However, the cryosurgical technique has not been completely established and long-term results of the procedure are still being evaluated.
- High intensity focused ultrasound (HIFU) is a procedure where the temperature inside the prostate is raised using a focused ultrasound beam. A probe placed in the rectum emits a beam of high intensity focused ultrasound. The sudden and intense absorption of the ultrasound beam quickly raises the temperature, which destroys prostate cancer cells. The published outcome data is limited, extending only to five years, and as such, HIFU is still considered experimental therapy and is only approved by the FDA for investigational use within the United States.
- Gene therapy or immune therapy may be successful in treating prostate cancer in the future. Current technology limits the use of these experimental treatments to a small number of medical centers.

Recurrent Prostate Cancer

If prostate cancer recurs following surgical removal of the prostate, then options for treatment include radiation therapy or medical management. Taking into account the time to recur following surgery and the radiology findings, your physician will determine whether the cancer is more likely to be localized or to have spread. If the cancer is thought to be localized, then external beam radiation therapy can be used with the goal of eradicating the cancer. If the cancer has spread, then medical management in the form of hormonal therapy or chemotherapy may be initiated.

If prostate cancer recurs following radiation, then options range from medical management, cryotherapy, surgical removal (salvage radical prostatectomy) and salvage radiation. A prostate biopsy is obtained to document recurrence and imaging is performed to rule out cancer spread. Treatment choice is based upon discussion with your physician, matching the potential for complications with the likelihood for cure to choose the best modality.

New in-roads are being made with regards to treatment of metastatic prostate cancer. Researchers have found a combination of cancer-fighting drugs that prolongs the life of men with advanced prostate cancer that no longer respond to hormone management. Cancer therapy combinations that include the cancer-fighting drug Taxotere increased the life span of cancer patients by almost 20%. Provenge, an experimental treatment vaccine for advanced prostate cancer, has recently demonstrated improved overall survival in clinical trials and is awaiting FDA approval.

Prevention

There's no sure way to prevent prostate cancer, but you can make some choices that might help reduce your risk. Experts know that diet and lifestyle choices play a part in prostate cancer risk. These steps may also help prevent other cancers and health conditions such as heart disease.

- Don't over-eat. Eat moderate-sized portions and keep your calories under control.
- Avoid high-fat foods. Prostate cancer rates vary greatly from one country to another, with the highest rates appearing in countries where people tend to eat a lot of fat. A diet high in saturated fats (such as animal fats found in red meat) may pose the greatest risk.
- Make healthy choices. Choose whole-grain foods, such as brown rice and whole-wheat bread. Limit sweets and salt.
- Drink alcohol in moderation. Generally, this means no more than two drinks a day for men.
- Eat a variety of fruits and vegetables. A diet high in fruits and vegetables has been linked to a lower risk of various kinds of cancer. Recent studies cast doubt on the theory that lycopene — an antioxidant found in tomatoes — lowers prostate cancer risk. But don't stop eating tomatoes. Eating plenty of all kinds of vegetables, including tomatoes, may help ward off prostate cancer and other cancers.
- Eat foods rich in omega-3 fatty acids. While a diet high in most kinds of fat is linked to a higher risk of cancer and other health problems, there is an exception. Omega-3 fatty acids — a type of fat found in cold-water fish such as salmon, herring and mackerel — appear to reduce the risk of certain cancers.
- Eat soy products and legumes. Soybeans and other legumes contain phytoestrogens, which are plant-based chemicals that behave like the hormone estrogen in the human body. These chemicals might help to prevent prostate cancer. In fact, one possible explanation for lower rates of prostate cancer in Asian men is that they eat more soy protein.
- Drink green tea. Green tea contains antioxidants such as polyphenols that may help prevent certain cancers and other health problems.
- Exercise. Researchers have not established a direct link between obesity and incidence of prostate cancer. However, there is a clear association of obesity with cancer risk, incidence, or progression for a number of common forms of cancer, and studies have shown that men who had been obese one year before prostate cancer diagnosis were 2.6 times more likely than men with a normal BMI to die of prostate cancer. So follow guidelines for a healthy diet, meet with your doctor to develop a plan for physical activity and do some form of aerobic exercise for 30 minutes or more daily.