

DIAGNOSIS OF PROSTATE CANCER

Determining the presence of prostate cancer generally involves a series of tests and exams. Before starting the testing process, the physician will ask questions about the medical history, family history of cancer and existing symptoms, and particularly problems with urination. From there, the doctor may proceed to any one of the tests described below.

Digital Rectal Exam (DRE)

Because the prostate lies in front of the rectum, the physician can feel the prostate by inserting a gloved, lubricated finger into the rectum. This simple procedure is called a digital rectal examination (DRE). It allows the physician to determine whether the prostate is enlarged or has lumps or other types of abnormal texture. While this examination may produce momentary discomfort, it should not cause significant pain.

Prostate Specific Antigen (PSA) Test

Used in addition to the digital rectal examination (DRE), a PSA test significantly increases the likelihood of early prostate cancer detection. PSA is the abbreviation for prostate specific antigen, a protein produced by the prostate cells and released into the blood stream. A PSA test measures the concentration of PSA in the bloodstream. Very little PSA escapes from a healthy prostate into the bloodstream, but certain prostate conditions can cause larger amounts of PSA to leak into the blood. Three possible causes of a high PSA level are: 1) a benign enlargement of the prostate called Benign Prostatic Hyperplasia (BPH), 2) Prostatitis (infection) or irritation in the area and 3) Prostate Cancer. An elevated level of PSA is a warning sign that prostate cancer may be present, but since other kinds of prostate disease can also cause high PSA levels, PSA testing by itself cannot confirm the presence of prostate cancer. A high PSA level only indicates the possibility of prostate cancer and the need for additional evaluation by the physician. Conversely, a low PSA level does not always mean that prostate cancer is not present. Although values differ by age, the standard cut-off point for a normal PSA is less than 4.0 ng/ml. Men younger than 50 should have a PSA less than 2.5 ng/ml. In addition, a rise in PSA of more than 1.0 ng/ml per year, regardless of the prior PSA may be significant. New studies suggest how fast the PSA doubles has also been found to be helpful. The significance of all of this is that the physician may not be using just one test or value, but rather a number of different methods to fully evaluate the

situation. It may even be necessary to reach back several years to compare old PSA levels to current ones. Men over the age of 40, and those men over the age of 35 who are in high-risk groups, such as African-American men and/or men with a family history of prostate cancer, should have a PSA blood test and digital rectal examination once every year. Any man who develops persistent urinary symptoms should contact his physician.

Biopsy

If the results of the digital rectal exam (DRE), the prostate specific antigen (PSA) tests are suspicious, a biopsy may be necessary. During the biopsy procedure, several small amounts of tissue are removed from the prostate with a needle. This tissue is then examined under a microscope for cancer cells. Only a biopsy can definitely confirm the presence or absence of prostate cancer. A biopsy of the prostate can be performed in the physician's office. Local anesthesia may be administered and the procedure takes about fifteen minutes. On average, 10-16 samples are taken. Keep in mind that it is still possible to have cancer, even if the biopsy is negative, because the needle, being tiny, may have missed a small focus of cancerous cells.

Grading of Tumors

If the biopsy is taken and prostate cancer is found, the pathologist will assign a grade to the lesion. A 5 point scale is typically used to classify the tumor, with 5 as the most aggressive (dangerous). The grade is determined by the characteristics under the microscope. The pathology report includes the two most common tumor grades encountered. After scanning several regions of biopsy material, the pathologist will report the two most common grades. This is reported as the sum of these two as: Gleason score: 4+3=7 (for example). The first number represents the most common pattern, while the second the next most common. In general, a Gleason's score of 2-6 is thought to represent a low-risk cancer, a Gleason Score of 7 represents a cancer of intermediate risk, and a cancer graded with a Gleason Score of 8-10 represents high-risk disease. The Gleason score is the most important predictor of the cancer's aggressiveness. Your physicians will also use this score to help them decide what is the best treatment.

STAGING OF PROSTATE CANCER

Once prostate cancer is discovered, the physician must estimate the size and extent of the cancer (how far it has already spread). This assessment is called staging of the tumor. Currently there are two different systems for staging prostate cancer. The traditional methods classify the disease into four clinical categories rated A through D. The second system is called TNM, which stands for Tumor-Nodes-Metastases, and is considered the most accepted staging system to date.

Staging is generally performed by digital rectal exam and is necessary for you and your physician to decide what type of treatment, if any, is most appropriate. Local stages include A or T1, B or T2 and C or T3. In addition to local staging within the prostate, an effort is also made to stage the extent of prostate cancer outside of the prostate as well. The most frequent areas of prostate cancer spread (metastasis) are to the surrounding lymph nodes (N+) and the bony skeleton (D or M+). For patients with high-grade, clinically high-stage disease or with a PSA > 10-20 ng/ml, a clinician may recommend a CT (computerized tomography) or bone scan to evaluate for external spread. These are generally not considered necessary in patients with low-risk disease.

PSA and percentage of biopsy cores found to harbor cancer are also important prognostic variables predicting prostate cancer outcome. In general, PSA values less than 10ng/ml indicates lower-risk disease, PSA values between 10-20 ng/ml are indicators of intermediate-risk disease, and PSA values higher than 20 are indicators of high-risk disease. In addition, if less than a third of all biopsy tissue submitted for microscopic review harbors cancer, the cancer is predicted to be of lower risk, if between 33 and 50% of the submitted tissue harbors cancer the disease is felt to be of intermediate risk, and if greater than 50% of the tissue submitted contains cancer, the cancer is considered higher risk. This biopsy risk stratification is additive to the risk status that would be assigned based on the stage, Gleason score and PSA.

Many tables and configurations have been developed that attempt to account for these four independently predictive variables and predict prognosis (tumor stage, grade, PSA and percentage of biopsy cores positive). In general, patients with low-risk features by all four measures are candidates for all treatment options (including watchful waiting in older patients, surgery, radiation, either external beam or radioactive seed placement (brachytherapy), as well as cryoablation (freezing). Patients considered intermediate risk are generally counseled against watchful waiting (if a 10-15 year life expectancy is predicted) Finally, men with

high-risk disease should understand that they have significant risk of cancer recurrence after treatment and that multiple types of treatments may be necessary.

A - D Staging System

- **Stage A** is early cancer. The tumor is located within the prostate gland and cannot be detected by a digital rectal examination.
- **In Stage B**, the tumor is considered to be within the prostate but is large enough to be felt during a digital rectal examination.
- **In Stage C**, prostate cancer is more advanced. It indicates that the tumor has spread outside the prostate to some surrounding areas, but has not spread to other organs. This stage of prostate cancer can usually be detected by a digital rectal examination.
- **In Stage D**, the cancer has spread to the nearby organs and usually to distant sites, such as the bones and/or lymph nodes (metastases).

TNM Staging

The Tumor-Node-Metastases (TNM) system breaks down the staging of prostate cancer into more categories than the A-D staging system does. As a result, the TNM system is much more complex and technical. The chart below lists all of the TNM stages. Your physician can tell you what TNM stage you have.

TNM Staging*

Primary Tumor, Clinical (T)

T0	No evidence of primary tumor
T1	Clinically not palpable or visible by imaging
T1a	Found incidental to other surgery; present in 5% or less of tissue
T1b	Found incidental to other surgery; present in 5% or more of tissue
T1c	Identified by needle biopsy
T2	Tumor confined within prostate
T2a	Involving half a lobe or less of prostate
T2b	Involving half a lobe
T2c	Involving both lobes
T3	Tumor extends through prostate capsule
T3a	Extends through one lobe or both lobes
T3b	Extends into seminal vesicles
T4	Tumor is fixed or invades adjacent structures other than seminal vesicles: bladder neck, external sphincter, rectum, levator muscles, and/or pelvic wall

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

Distant Metastases - (M)

- MX Distant metastasis cannot be assessed
- M0 No distant metastasis
- M1 Distant metastasis
- M1a Non-regional lymph node(s)
- M1b Bone(s)
- M1c Other site(s)

PROSTATE CANCER TREATMENT OPTIONS

Over the past 20 years, overall survival rates for all stages of prostate cancer combined have increased significantly. Some of the possible reasons for the increase in survival rates include public education, new techniques of early detection, and better medical therapies. The major treatment options for prostate cancer include: surgery, radiation, medical therapy, a combination of medical therapy and surgery or radiation, chemotherapy, cryoablation and watchful waiting. A patient's treatment options will depend upon his age, grade of disease, PSA level, the stage of the disease, and the advice of a physician.

Surgery for Prostate Cancer

The goal of surgery is to remove the entire prostate gland, seminal vesicles and all of the cancer. What follows is a description of a number of techniques used by surgeons when operating on the prostate.

The Radical Prostatectomy

The surgical removal of the entire prostate gland is called radical prostatectomy. Radical prostatectomy is usually performed to remove early-stage prostate cancer before it can spread to other parts of the body. Often, the pelvic lymph nodes are also sampled for a biopsy as a precautionary measure. Patients who undergo radical prostatectomy should expect at least a 1- to 3- day stay in the hospital, while full recovery takes 4-6 weeks. As with all major surgeries, some prostatectomy patients may require a blood transfusion. Rarely, hormonal therapy is used before surgery to shrink the prostate cancer so it can be removed more effectively. The nerve-sparing approach to prostatectomy has reduced the rate of incontinence and erectile dysfunction dramatically following surgery.

Robotic and Laparoscopic Prostatectomy

Surgery can be performed with the laparoscope (with small instruments) as well as through a small incision above the pubic bone. With laparoscopic surgery an incision large enough to remove the prostate (2-3inches) is still required to remove the prostate after it has been dissected from the body. Laparoscopic surgery may be performed with or without the assistance of an operating robot (DaVinci System). The usual hospital stay following robotic or laparoscopic radical

prostatectomy is 1-2 nights. One of the most important factors to consider when evaluating surgery as an option for prostate cancer is the surgeon. Studies have clearly shown that those surgeons more experienced with a particular operation are more likely to have positive outcomes. The cancer cure and side effects associated with the prostatectomy procedures are all similar regardless of the type of procedure performed (open, laparoscopic, or robotic).

External Beam Radiation Therapy/Brachytherapy Seeds

Radiation therapy involves exposing cancer cells to high doses of radiation to kill the tumor. The most widely used types are external beam radiation therapy and internal radiation therapy (brachytherapy). External beam radiation therapy treats the prostate and other selected tissues with a carefully targeted beam of radiation administered from machines outside the body. Brachytherapy or interstitial therapy, tiny radioactive seeds are implanted in the prostate through a surgical procedure. The newest technology for external beam radiation therapy is IGRT or image guided radiation therapy. Both IGRT and brachytherapy allow the physicians to increase the dose of radiation to the tumor and with a lower risk of damage to the tissues near the prostate (rectum, bladder and nerve supply). Higher doses of radiation are necessary when patients have intermediate and high risk disease. Sometimes your physician may recommend a combination of IGRT and brachytherapy. These recommendations are often made to patients with the highest risk prostate cancer.

External beam radiation is sometimes recommended after prostatectomy. Recent studies have found a benefit to adding radiation therapy after prostatectomy when the pathologist has determined the cancer has spread outside of the gland. In such cases the radiation is usually started 2-3 months after the prostatectomy (adjuvant radiation). Following the prostatectomy, the PSA is usually <0.2 ng/ml. A slowly rising PSA after a prostatectomy may indicate a local recurrence. Patients with a local recurrence following prostatectomy may also be good candidates for radiation therapy (salvage radiation).

Cryoablation

Cryoablation has undergone significant evolution since its initial use. Some advances include the use of transrectal ultrasound monitoring, temperature-sensing thermocouples, and a urethral warming device. Longer term data has recently become available suggesting this treatment may be as effective as the

others in certain clinical situations. Cryoablation can also be used in cases where cancer has recurred following radiation (either external beam or brachytherapy). Following radiation therapy the PSA usually decreases to a low value (<0.5 ng/ml). A transient increase (PSA bounce) can happen in almost 50% of patients following radiation treatment. This bounce can happen 1-3 years following the treatment. An increase of 2 ng/ml is considered a failure. If you have received radiation therapy and your PSA has risen more than this amount you may want to speak to your physician about performing a prostate biopsy. If the biopsy is positive (showing persistent cancer) you may be a candidate for salvage cryoablation. Prostate cryoablation is performed in the operating room with one night hospital stay or as an outpatient procedure.

Side Effects of Local Treatment

All treatments for localized prostate cancer carry some risk of complications. The most common side effects include impotence and incontinence (involuntary loss of urine). In general, these side effects are more common with surgery than with radiation. However, impotence and incontinence tend to appear later when radiation is used, whereas, they are more pronounced immediately after surgery. Some studies suggest that with long follow-up, long term complications may only be minimally different between all of the different treatment choices. The individual expertise of the surgeon, radiotherapist or brachytherapist is one of the most important factors contributing to a positive outcome.

Watchful Waiting

Watchful waiting is another option involving careful observation without immediate treatment for prostate cancer. This may be an appropriate therapeutic course for men who:

- Are found to have low risk or less aggressive tumors, which often tend to grow slowly
- Have a life expectancy less than 10-15 years
- Have significant coexisting illnesses
- Are fearful of the side effects of more aggressive therapies

Patients electing watchful waiting will need regular careful observation of their cancers. This may require frequent PSA testing and repeat prostate biopsies.

Hormones (Androgen Deprivation), Bisphosphonates, and Prostate Cancer

Hormonal therapy results in a decrease in the male hormone (testosterone) to castrate levels. In the past, female hormones were used to achieve this goal. Today medications can lower testosterone levels without the side effects of female hormones (estrogen). Hormonal therapy is sometimes used before radiation therapy to shrink the prostate and the tumor. The smaller prostate may allow the radiation to be more tightly focused, concentrating the dose so that the tumor receives more rays. Studies demonstrate that the combination of hormone therapy with radiation increase cure and survival rate in patients with more aggressive prostate cancer. Hormone therapy (also called androgen deprivation) is also used for palliative care in patients with very advanced or recurrent prostate cancer. When hormone therapy is used testosterone levels decrease (like castration), the tumor shrinks and PSA levels generally drop, often to undetectable (< 0.1 ng/ml). In patients with metastases, the disease can be stabilized and most patients will go into remission, usually for many years.

Oral and injectable agents are used in achieving androgen deprivation. Injectable agents, in general, are classified as leutinizing-hormone releasing hormone (LHRH) agonist. These agonists alter the signal that causes testosterone production and are available in intramuscular and subcutaneous pellet forms and are given at monthly, quarterly, longer intervals. The main side effects of LHRH agonists include hot flashes and erectile dysfunction (loss of erection). Additional complaints include fatigue, mental status changes, decreased muscle mass, increased body fat, and osteoporosis with extended use. Despite these drawbacks, many patients tolerate LHRH agonist therapies for many years without difficulty.

Oral medications called anti-androgens block the action of testosterone circulating in the bloodstream. Anti-androgens can be taken with injectable LHRH agonists, at the initiation of LHRH agonist treatment, or as a solitary treatment for prostate cancer. The advantage of using both LHRH agonists and anti-androgen medications together is a more complete control of the cancer. Anti-androgens should always, however, be used at the initiation of LHRH injections. LHRH agonists when used alone can cause a flare in the serum testosterone which can have significant negative side effects. You should discuss with your physician which medications would best for your individual situation.

Androgen Independent Prostate Cancer and Clinical Trials

Once a patient has been on androgen deprivation treatment for an extended period of time, prostate cancer may progress in spite of androgen deprivation. In this scenario, low serum testosterone levels are verified and anti-androgen tablets are added if they have not been used in the past. If a patient has been taking anti-androgen tablets, these are either discontinued or switched, as rarely anti-androgen tablets can serve to increase the activity of the androgen receptor. Once these conservative measures have been tried and failed, a patient is considered to have “androgen independent prostate cancer.” This condition is also referred to as hormone refractory prostate cancer. Certain chemotherapeutic combinations have been shown to improve survival in androgen independent prostate cancer, such as docetaxol. Mitoxantrone and prednisone has also been used in this setting and has been shown to improve the quality of life in patients with this condition. Newer chemotherapeutic agents, gene therapy and immunotherapy are constantly being tested. You may be a good candidate for a clinical trial if this situation arises. You should speak to your physician about all options should you develop hormone refractory disease.

THE VALUE OF EARLY DETECTION

Detection of the disease when it is at an early stage offers the best opportunity for successful treatment of prostate cancer. In other words, if the disease is diagnosed when it is confined to the prostate and is treated promptly, complete recovery can be achieved. This means having your physician check you for prostate cancer yearly, if you are 40 years of age or older or if you are 35 years of age and are considered to be at high risk.

You are at high risk for prostate cancer if one or more of the following factors pertain to you:

- African-American race
- Increasing age
- Family history of prostate cancer
- A high-fat diet

PROSTATE CANCER PREVENTION/RESEARCH

There is a great deal of active research on the prevention of prostate cancer. Although clinical trials are still not conclusive, many individuals believe that a low fat diet rich with lycopene foods and supplements such as selenium and vitamin E may help prevent prostate cancer.

Lycopene /Vitamin E/Selenium/Supplements

Lycopene is the antioxidant that gives tomatoes and other fruits their red color. Cooking the tomatoes breaks down the cell walls, allowing your body to access the lycopene much easier than from fresh tomatoes. Some studies have suggested prostate cancer may be reduced in men who consume large amounts of lycopene. Be sure to consult your physician about any changes you make to your diet. Recent studies have shown that vitamin E and selenium supplements may have some health benefits with respect to the prevention of prostate cancer. Multivitamins and supplements contain compounds that can interfere with the successful outcomes of your prostate cancer treatment. For example, vitamin E can increase bleeding, which could complicate prostate cancer surgery. Antioxidants can interfere with the efficacy of radiation. The current recommendations are to stop all vitamins and supplements 2 weeks before surgery and during the entire course of radiation therapy. You should discuss your vitamins and supplement intake with your physician before any treatments.

WHAT TO ASK YOUR DOCTOR

Talking to your doctor is one of the best ways to help you understand your medical condition. When sitting in your doctor's office, it can be hard to remember all the questions that you may have. Sometimes it is helpful to write down a list of concerns to discuss with your physician.

WHAT TO ASK ABOUT PROSTATE CANCER

If you have been diagnosed with prostate cancer, you and your family probably have a lot of questions about the disease and its treatment. Printing out this list and taking it with you to your doctor's office may help you get the answers you

need. Be sure to write out the answers, so that you can review the information as often as you like.

- What grade and stage is my prostate cancer?
- What are my treatment options?
- Can it be cured?
- What are the advantages or disadvantages of both medical, radiation and surgical therapies?
- What are the side effects of:
 - Surgery?
 - Radiation?
 - Brachytherapy?
 - Cryoablation?
 - Hormonal therapy?
- Is watchful waiting safe?
- How does one cope with prostate cancer?
- What if the prostate cancer comes back after my initial treatment?
- How can I receive more information on prostate cancer?
- What will my future look like after treatment?
- Should my family members get screened for prostate cancer?
- Can I get a second opinion?

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