



## PROSTATE CANCER

### What is cancer?

Cancer develops when cells in a part of the body begin to grow out of control. Although there are many kinds of cancer, they all start because of out-of-control growth of abnormal cells.

Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide more rapidly until the person becomes an adult. After that, cells in most parts of the body divide only to replace worn-out or dying cells and to repair injuries.

Because cancer cells continue to grow and divide, they are different from normal cells. Instead of dying, they outlive normal cells and continue to form new abnormal cells.

Cancer cells develop because of damage to DNA. This substance is in every cell and directs all its activities. Most of the time when DNA becomes damaged the body is able to repair it. In cancer cells, the damaged DNA is not repaired. People can inherit damaged DNA, which accounts for inherited cancers. Many times though, a person's DNA becomes damaged by exposure to something in the environment, like smoking.

Cancer usually forms as a tumor. Some cancers, like leukemia, do not form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

Often, cancer cells travel to other parts of the body, where they begin to grow and replace normal tissue. This process is called metastasis. Regardless of where a cancer may spread, however, it is always named for the place it began. For instance, breast cancer that spreads to the liver is still called breast cancer, not liver cancer.

Not all tumors are cancerous. Benign (non-cancerous) tumors do not spread (metastasize) to other parts of the body and, with very rare exceptions, are not life threatening.

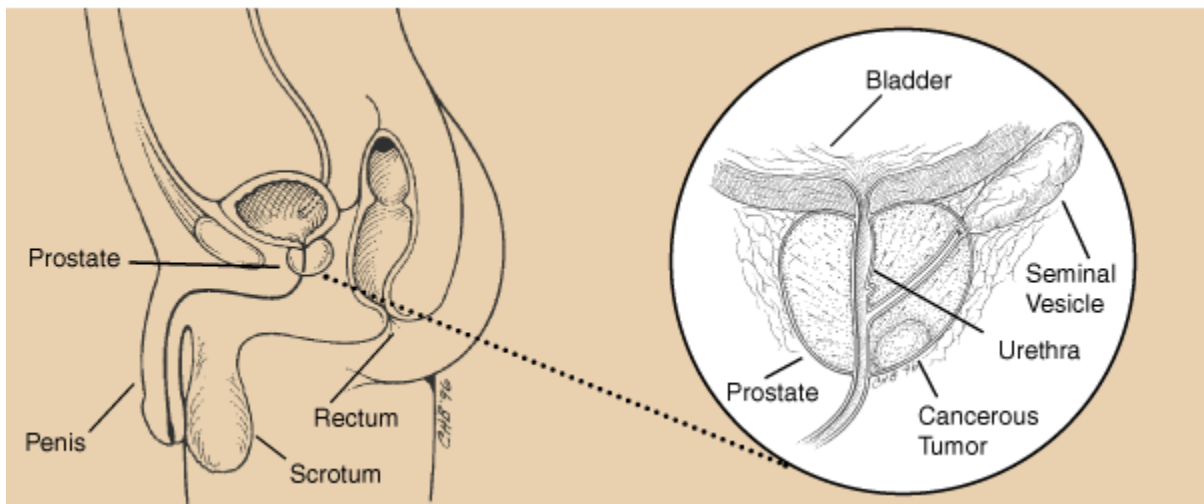
Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer.

Cancer is the second leading cause of death in the United States. Nearly half of all men and a little over one third of all women in the United States will develop cancer during their lifetimes. Today, millions of people are living with cancer or have had cancer. The risk of developing most types of cancer can be reduced by changes in a person's lifestyle, for example, by quitting smoking and eating a better diet. The sooner a cancer is found and treatment begins, the better are the chances for living for many years.

## What Is Prostate Cancer?

### About the Prostate

Only men have a prostate. As shown in the picture below, it's a walnut-sized gland located in front of the rectum and underneath the urinary bladder. The prostate's job is to make some of the fluid that protects and nourishes sperm cells in semen. Just behind the prostate gland are the seminal vesicles that make most of the fluid for semen. The urethra, which is the tube that carries urine and semen out of the body through the penis, runs through the prostate.



The prostate starts to develop before birth and continues to grow until a man reaches adulthood. This growth is fueled by male hormones (called androgens) in the body. The main androgen is testosterone. The prostate stays about the same size in adults as long as male hormones are present. In older men, the inner part of the prostate around the urethra may continue to grow, a condition called *benign prostatic hyperplasia (BPH)*. While this can cause problems with urinating because it can press on the urethra (the tube that carries the urine), BPH is not cancer.

## Prostate Cancer

Although several types of cells are found in the prostate, over 99% of prostate cancers develop from the gland cells. Gland cells make the prostate fluid that is added to the semen. The medical term for a cancer that starts in gland cells is *adenocarcinoma*.

Other types of cancer can also start in the prostate gland, including sarcomas, small cell carcinomas, and transitional cell carcinomas. But because these other types of prostate cancer are so rare, if you have prostate cancer it is almost certain to be an adenocarcinoma. **The rest of this document refers only to prostate adenocarcinoma.**

While some prostate cancers can grow and spread quickly, most prostate cancers grow slowly. In fact, autopsy studies show that many older men (and even some younger men) who died of other diseases also had prostate cancer that never affected them during their lives. In these studies, 70% to 90% of the men had cancer in their prostate by age 80, but in many cases neither they nor their doctors even knew they had it.

## Pre-cancerous Conditions of the Prostate

Many doctors believe that prostate cancer begins with a pre-cancerous condition called *prostatic intraepithelial neoplasia (PIN)*. PIN begins to appear in the prostates of some men as early as their 20s. Almost half of all men have PIN by the time they reach 50. In this condition, there are changes in how the prostate gland cells look under the microscope, but the cells are basically still in place -- they don't look like they've invaded other parts of the prostate (like cancer cells would). The changes are classified as either low-grade, meaning the patterns of prostate cells appear almost normal, or high-grade, meaning they look more abnormal.

If you have had high-grade PIN found on a prostate biopsy, there is about a 20% chance that you also have cancer in your prostate. For this reason, doctors often watch men with high-grade PIN carefully and may advise a repeat prostate biopsy, especially if the original biopsy did not take samples from all parts of the prostate.

Another finding that may be reported on a prostate biopsy is *atypical small acinar proliferation (ASAP)*, which is sometimes just called *atypia*. In ASAP, the cells look like they might be cancerous when viewed under the microscope, but there are too few of them on the slide to be sure. If ASAP is found, there's about a 40% to 50% chance that cancer is also present in the prostate, which is why many doctors advise getting a repeat biopsy within a few months.

## What Are the Key Statistics About Prostate Cancer?

Prostate cancer is the most common cancer, other than skin cancers, in American men. The American Cancer Society estimates that during 2008 about 186,320 new cases of prostate cancer will be diagnosed in the United States. About 1 man in 6 will be diagnosed with prostate cancer during his lifetime, but only 1 man in 35 will die of it. More than 2 million men in the United States who have been diagnosed with prostate cancer at some point are still alive today.

Prostate cancer is the second leading cause of cancer death in American men, behind only lung cancer. The American Cancer Society estimates that 28,660 men in the United States will die of prostate cancer in 2008. Prostate cancer accounts for about 10% of cancer-related deaths in men.

More than 9 out of 10 prostate cancers are found in the local and regional stages (local means it is still confined to the prostate; regional means it has spread from the prostate to nearby areas, but not to distant sites, such as bone). When compared to men the same age and race who do not have cancer (called relative survival), the 5-year relative survival rate for these men is nearly 100%.

The 5-year relative survival rate for men whose prostate cancers have already spread to distant parts of the body at the time of diagnosis is about 32%.

Five-year survival rates refer to the percentage of men who live *at least* 5 years after their prostate cancer is first diagnosed. Keep in mind that many patients live much longer than 5 years after diagnosis. *Relative* survival rates compare the observed survival with that expected for people without prostate cancer. That means that relative survival refers **only** to deaths from prostate cancer. Because prostate cancer usually occurs in older men who often have other health problems, relative survival rates are generally used to produce a standard way of discussing *prognosis* (outlook).

To measure 10-year survival rates, we must have records of patients diagnosed more than 10 years ago. According to the most recent data, for all men with prostate cancer, the relative 10-year survival rate is 91% and the 15-year survival rate is 76%. Modern methods of detection and treatment mean that prostate cancers are now found earlier and treated more effectively. If you are diagnosed this year, your outlook is likely to be better than the numbers reported above.

## What Are the Risk Factors for Prostate Cancer?

A risk factor is anything that affects your chance of getting a disease such as cancer. Different cancers have different risk factors. For example, exposing skin to strong sunlight is a risk factor for skin cancer. Smoking is a risk factor for cancers of the lungs, mouth, throat, larynx (voice box), bladder, and several other organs.

But risk factors are not absolute. Many people with one or more risk factors never get cancer, while others with this disease may have had no known risk factors.

Although we don't yet completely understand the causes of prostate cancer, researchers have found several factors that increase the risk of getting it.

### Age

Age is the strongest risk factor for prostate cancer. Prostate cancer is very rare before the age of 40, but the chance of having prostate cancer rises rapidly after age 50. About 2 out of 3 prostate cancers are found in men over the age of 65.

## **Race/Ethnicity**

Prostate cancer occurs more often in African-American men than in men of other races. African-American men are also more likely to be diagnosed at an advanced stage, and are more than twice as likely to die of prostate cancer as white men. Prostate cancer occurs less often in Asian-American and Hispanic/Latino men than in non-Hispanic whites. The reasons for these racial and ethnic differences are not clear.

## **Nationality**

Prostate cancer is most common in North America, northwestern Europe, Australia, and on Caribbean islands. It is less common in Asia, Africa, Central America, and South America. The reasons for this are not clear. More intensive screening in some developed countries likely accounts for at least part of this difference, but other factors are likely to be important as well. For example, lifestyle differences (diet, etc.) may be important: men of Asian descent living in the United States have a lower risk of prostate cancer than white Americans, but their risk is higher than that of men of similar backgrounds living in Asia.

## **Family History**

Prostate cancer seems to run in some families, which suggests that in some cases there may be an inherited or genetic factor. Having a father or brother with prostate cancer more than doubles a man's risk of developing this disease. (The risk is higher for men with an affected brother than for those with an affected father.) The risk is much higher for men with several affected relatives, particularly if their relatives were young at the time the cancer was found.

Scientists have found several inherited genes that seem to raise prostate cancer risk (see section, "Do We Know What Causes Prostate Cancer?"), but they probably account for only a small number of cases overall. Genetic testing for these genes is not yet available.

Some inherited genes raise the risk for more than one type of cancer. For example, inherited mutations of the BRCA1 or BRCA2 genes are the reason that breast and ovarian cancers are much more common in some families. The presence of these gene mutations may also increase prostate cancer risk in some men, but they account for a very small percentage of prostate cancer cases.

## **Diet**

The exact role of diet in prostate cancer is not clear, although several different factors have been studied.

Men who eat a lot of red meat or high-fat dairy products appear to have a slightly higher chance of getting prostate cancer. These men also tend to eat fewer fruits and vegetables. Doctors are not sure which of these factors is responsible for raising the risk.

Some studies have suggested that men who consume a lot of calcium (through food or supplements) may have a higher risk of developing advanced prostate cancer. Most studies have not found such a link with the levels of calcium found in the average diet, and it's important to note that calcium is known to have other important health benefits.

## **Factors With Uncertain, Controversial, or Unproven Effects on Prostate Cancer Risk**

### **Obesity**

Most studies have not found that being obese is linked with a higher risk of getting prostate cancer. But several studies have found that obese men may be at greater risk for having more advanced prostate cancer and of dying from prostate cancer. The reasons for this are not clear.

### **Exercise**

In most studies, exercise has not been shown to reduce prostate cancer risk. But some studies have found that high levels of physical activity, particularly in older men, may lower the risk of advanced prostate cancer. More research in this area is needed.

### **Infection and Inflammation of the Prostate**

Some studies have suggested that prostatitis (inflammation of the prostate gland) may be linked to an increased risk of prostate cancer. Inflammation is often seen in samples of prostate tissue that also contain cancer. While the link between the two is not yet clear, this is an active area of research.

Some researchers have also looked at the possibility that sexually transmitted infections might increase the risk of prostate cancer, possibly by leading to inflammation of the prostate. But this has been a difficult area to study, and no firm conclusions have been reached.

### **Vasectomy**

Some earlier studies had suggested that men who had a vasectomy (minor surgery to make men infertile) -- especially those younger than 35 at the time of the procedure -- may have a slightly increased risk for prostate cancer. But most recent studies have not found any increased risk among men who have had this operation. Fear of an increased risk of prostate cancer should not be a reason to avoid a vasectomy.

## **Do We Know What Causes Prostate Cancer?**

We still do not know exactly what causes prostate cancer. But researchers have found some risk factors and are trying to learn just how these factors cause prostate cells to become cancerous (see section, "What Are the Risk Factors for Prostate Cancer?").

On a basic level, prostate cancer is caused by changes in the DNA of a prostate cancer cell. During the past few years, scientists have made great progress in understanding how certain changes in DNA can cause normal prostate cells to grow abnormally and form cancers. DNA

is the chemical that carries the instructions for nearly everything our cells do. The reason that you might look like your parents is because they are the source of your DNA.

DNA affects more than the way you look. Some genes (parts of your DNA) contain instructions for controlling when cells grow and divide. Certain genes that promote cell growth and division are called *oncogenes*. Others that normally slow down cell division or cause cells to die at the right time are called *tumor suppressor genes*. Cancer can be caused by DNA changes (mutations) that turn on oncogenes or turn off tumor suppressor genes.

DNA changes can either be inherited from a parent or can be acquired during a person's lifetime.

### **Inherited DNA Mutations**

Researchers have found inherited DNA changes in certain genes may cause about 5% to 10% of prostate cancers.

Several mutated genes have been found that may be responsible for a man's inherited tendency to develop prostate cancer. One of these is called HPC1 (**H**ereditary **P**rostate **C**ancer **G**ene **1**). But there are many other gene mutations that may account for some cases of hereditary prostate cancer. None of these is a major cause, and more research on these genes is being done. Genetic tests are not yet available.

As mentioned above, men with BRCA1 or BRCA2 gene changes may have an increased prostate cancer risk. But BRCA changes are believed to explain only a very small number of prostate cancers.

### **DNA Mutations Acquired During a Man's Lifetime**

Most DNA mutations related to prostate cancer seem to develop during a man's life rather than having been inherited. Every time a cell prepares to divide into 2 new cells, it must copy its DNA. This process is not perfect, and sometimes errors occur, leaving the flawed DNA in the new cell.

It is not clear how many of these DNA mutations might be random events, and how many may be influenced by other factors (diet, hormone levels, etc.). In general, the more quickly prostate cells grow and divide, the more chances there are for mutations to occur. Therefore, anything that speeds up this process may make prostate cancer more likely.

The development of prostate cancer may be linked to increased levels of certain hormones. High levels of androgens (male hormones, such as testosterone) promote prostate cell growth, and may contribute to prostate cancer risk in some men.

Some researchers have noted that men with high levels of another hormone, insulin-like growth factor-1 (IGF-1), are more likely to get prostate cancer. IGF-1 hormone is similar to insulin, but it works on cell growth, not sugar metabolism. However, other studies have not

found a link between IGF-1 and prostate cancer. Further research is needed to make sense of these findings.

As mentioned in the "What Are the Risk Factors for Prostate Cancer?" section, some recent studies have found that inflammation may contribute to prostate cancer. One theory is that inflammation may lead to cell DNA damage, which might in turn push a cell closer to becoming cancerous. More research in this area is needed.

Exposure to radiation or cancer-causing chemicals may cause DNA mutations in many organs of the body, but these factors have not been proven to be important causes of mutations in prostate cells.

## Can Prostate Cancer Be Prevented?

Because the exact cause of prostate cancer is not known, at this time it is not possible to prevent most cases of the disease. Many risk factors such as age, race, and family history cannot be controlled. But based on what we do know, some cases might be prevented.

### Diet

While the results of research studies are not yet clear, you may be able to reduce your risk of prostate cancer by changing the way you eat.

The American Cancer Society recommends choosing foods and beverages in amounts that help achieve and maintain a healthy weight, eating a variety of healthful foods with an emphasis on plant sources, and limiting your intake of red meats, especially high-fat or processed meats. Eat 5 or more servings of fruits and vegetables each day. Whole-grain breads, cereals, rice, pasta, and beans are also recommended. These guidelines on nutrition may also lower the risk for some other types of cancer, as well as other health problems.

Tomatoes (raw, cooked, or in tomato products such as sauces or ketchup), pink grapefruit, and watermelon are rich in *lycopenes*. These vitamin-like substances are antioxidants that help prevent damage to DNA. Some earlier studies suggested lycopenes may help lower prostate cancer risk, although a more recent study found no link between blood levels of lycopene and risk of prostate cancer. Research in this area continues.

Taking vitamin or mineral supplements may affect your prostate cancer risk, but this is not yet clear. Some studies suggest that taking 50 milligrams (or 400 International Units) of vitamin E daily can lower risk. But other studies have found that vitamin E supplements have no impact on cancer risk, and larger doses may increase risk for some kinds of heart diseases. Selenium, a mineral, may also lower risk. On the other hand, beta-carotene supplements may actually raise prostate cancer risk. Taking any supplements can have risks and benefits. Before starting vitamins or other supplements, you should talk with your doctor.

The possible effects of selenium and vitamin E on prostate cancer risk are now being studied in the Selenium and Vitamin E Cancer Prevention Trial (SELECT). This large clinical trial is under way, but the results will probably not be available for several years.



Several studies are now looking at the possible effects of soy proteins (called isoflavones) on prostate cancer risk. The results of these studies are not yet available.

## Medicines

Some drugs may also help reduce the risk of prostate cancer.

*Finasteride* (Proscar) is a drug already used to treat benign prostatic hyperplasia (BPH). It works by preventing the body from making a certain potent androgen (male hormone).

A large clinical trial (the Prostate Cancer Prevention Trial, or PCPT) tested taking finasteride versus a placebo (sugar pill) each day for 7 years. At the end of the study, men taking finasteride were less likely to have prostate cancer than those getting the placebo. But the cancers that did develop in the men taking finasteride looked like they were more likely to grow and spread. The reason for this is not known. Researchers are still watching these men to see if these cancers really do grow and spread more quickly.

Finasteride was more likely to cause sexual side effects such as lowered sexual desire and impotence. But it seemed to help with urinary problems such as trouble urinating and leaking urine (incontinence).

At this time, not all doctors agree whether taking finasteride to prevent prostate cancer is a good thing. Men thinking about this should discuss it with their doctors. The results of the PCPT will become clearer over the next few years.

Other drugs that may help prevent prostate cancer are now being tested in clinical trials. These include anti-inflammatory drugs such as celecoxib and drugs that affect hormone levels such as toremifene.

## Can Prostate Cancer Be Found Early?

Prostate cancer can often be found early by testing the amount of *prostate-specific antigen* (PSA), discussed in detail below, in your blood. Prostate cancer may also be found on a *digital rectal exam* (DRE), in which your doctor inserts a gloved finger into the rectum. Because your prostate gland lies just in front of your rectum, the doctor can feel whether there are any bumps or hard areas in your prostate. If there are, you will need further testing to see if there is a cancer. If you have routine yearly exams and either one of these test results becomes abnormal, then any cancer you might have has likely been found at an early, more treatable stage.

Since the use of early detection tests for prostate cancer became fairly common (about 1990), the prostate cancer death rate has dropped. But it has not been proven that this is a direct result of screening.

There are limits to the current screening methods. Neither the PSA test nor the DRE is 100% accurate. Uncertain or false test results could cause confusion and anxiety. Some men might

have a prostate biopsy (which carries its own small risks, along with discomfort) when cancer is not present, while others might get a false sense of security from normal test results when cancer is actually present.

There is no question that the PSA test can help spot many prostate cancers early, but another important issue is that it can't tell how dangerous the cancer is. Finding and treating all prostate cancers early may seem like a no-brainer. But some prostate cancers grow so slowly that they would likely never cause problems. Because of an elevated PSA level, some men may be diagnosed with a prostate cancer that would never have caused any symptoms or lead to their death. But they may still be treated with either surgery or radiation, either because the doctor can't be sure how aggressive the cancer might be, or because the men are uncomfortable not having any treatment. These treatments can have side effects that seriously affect a man's quality of life. Doctors and patients are still struggling to decide who should receive treatment and who might be able to be followed without being treated right away (an approach called "watchful waiting" or "expectant management").

Until more information is available, whether you have the tests is something for you and your doctor to decide. There are many factors to take into account, including your age and health. If you are young and develop prostate cancer, it will probably shorten your life if it is not caught early. If you are older or in poor health, then prostate cancer may never become a major problem because it is generally a slow-growing cancer.

### **ACS Recommendations for the Early Detection of Prostate Cancer**

The American Cancer Society believes that health care professionals should *offer* the prostate-specific antigen (PSA) blood test and digital rectal exam (DRE) yearly, beginning at age 50, to men who have at least a 10-year life expectancy. Men at high risk, such as African Americans and men who have a first-degree relative (father, brother, or son) diagnosed with prostate cancer at an early age (younger than age 65), should begin testing at age 45.

Men at even higher risk (because they have several first-degree relatives who had prostate cancer at an early age) could begin testing at age 40. Depending on the results of this initial test, further testing might not be needed until age 45.

Health care professionals should give men the chance to openly discuss the benefits and limitations of testing at yearly checkups. Men should actively take part in the decision by learning about prostate cancer and the pros and cons of early detection and treatment of prostate cancer.

### **Recommendations of Other Organizations**

No major scientific or medical organizations, including the American Cancer Society (ACS), American Urological Association (AUA), US Preventive Services Task Force (USPSTF), American College of Physicians (ACP), National Cancer Institute (NCI), American Academy of Family Physicians (AAFP), and American College of Preventive Medicine (ACPM) support routine testing for prostate cancer at this time. The USPSTF has concluded that

studies completed so far do not provide enough evidence to know whether the benefits of testing for early prostate cancer outweigh the possible risks.

The ACS, AUA, ACP, NCI, AAFP, and ACPM recommend that health care professionals discuss the possible benefits, side effects, and questions about early prostate cancer detection and treatment so that men can make informed decisions taking into account their own situation and risk. In addition, the American Cancer Society and the American Urological Association recommend that health care professionals offer the option of testing for early detection of prostate cancer to all men who are at least 50 years old (or younger if at higher risk).

## Prostate-Specific Antigen (PSA) Blood Test

Prostate-specific antigen (PSA) is a substance made by cells in prostate gland (whether they are normal or cancerous). Although PSA is mostly found in semen, a small amount is also found in the blood. Most men have levels under 4 nanograms per milliliter (ng/mL) of blood.

When prostate cancer develops, the PSA level usually goes above 4. But about 15% of men with a PSA below 4 will have prostate cancer on biopsy. If your PSA level is in the borderline range between 4 and 10, you have about a 1 in 4 chance of having prostate cancer. If it is more than 10, your chance of having prostate cancer is over 50% and increases more as your PSA level increases.

The PSA level can also be affected by a number of factors other than prostate cancer:

- It rises with non-cancerous enlargement of the prostate (called *benign prostatic hyperplasia*, or BPH), something many men have as they grow older.
- It can also increase with *prostatitis*, an infection or inflammation of the prostate gland.
- Your PSA will also normally go up slowly as you *age*, even if you have no prostate abnormality.
- *Ejaculation* can cause a temporary increase in blood PSA levels, so some doctors will suggest that men abstain from ejaculation for 2 days before testing.
- Some *medicines* used to treat BPH or urinary symptoms may affect blood PSA levels. You should tell your doctor if you are taking finasteride (Proscar or Propecia) or dutasteride (Avodart), as these medicines may falsely lower PSA levels and require the doctor to adjust the reading.
- *Herbal mixtures* that are sold as dietary supplements "for prostate health" may affect PSA levels. For example, they could mask a high PSA level. This is why it is important to let your doctor know if you are taking any type of supplement. Saw palmetto (an herb used by some men to treat BPH) does not seem to interfere with the measurement of PSA.

If your PSA level is high, your doctor may advise a prostate biopsy (see section, “How Is Prostate Cancer Diagnosed?”) to find out if you have cancer. Some doctors may consider using newer types of PSA tests (discussed below) to help determine if you need a prostate biopsy, but not all doctors agree on how to use these other PSA tests. If your PSA test result is not normal, ask your doctor to discuss your cancer risk and your need for further tests.

### **Percent-free PSA**

PSA occurs in 2 major forms in the blood. One form is attached to blood proteins while the other circulates free (unattached). The percent-free PSA (fPSA) is the ratio of how much PSA circulates free compared to the total PSA level. The percentage of free PSA is lower in men who have prostate cancer than in men who do not.

This test is sometimes used to help decide if you should have a prostate biopsy if your PSA results are in the borderline range (4-10 ng/mL). A lower percent-free PSA means that your likelihood of having prostate cancer is higher and you should probably have a biopsy. Many doctors recommend biopsies for men whose percent-free PSA is 10% or less, and advise that men consider a biopsy if it is between 10% and 25%. Using these cutoffs detects most cancers while helping some men to avoid unnecessary prostate biopsies. Although this test is widely used, not all doctors agree that 25% is the best "cutoff point" to decide on a biopsy.

A newer test, known as *complexed PSA*, measures the amount of PSA that is attached to other proteins. This test is described in more detail in the section, "What's New in Prostate Cancer Research and Treatment?"

### **PSA Velocity**

The PSA velocity is not a separate test. It is a measure of how fast the PSA rises over time. Even when the total PSA value isn't over 4 ng/mL, a high PSA velocity suggests that cancer may be present and a biopsy should be considered. For example, if your PSA was 1.7 on one test, and then a year later it was 3.8, this rapid rise may be cause for concern.

This can be useful if you are having the PSA test every year. For men whose initial PSA value is less than 4, a PSA velocity of 0.35 ng/mL per year or greater (for example, if values went from 2 to 2.4 to 2.8 over the course of 2 years) may be cause for concern. For men whose PSA value is between 4 and 10, a biopsy should be more strongly considered if it goes up faster than 0.75 ng/mL per year (for example, if values went from 4 to 4.8 to 5.6 over the course of 2 years). Most doctors believe that PSA levels should be measured on at least 3 occasions over a period of at least 18 months in order to get an accurate PSA velocity.

### **PSA Density**

PSA levels are higher in men with larger prostate glands. The PSA density (PSAD) is sometimes used for men with large prostate glands to try to adjust for this. The doctor measures the volume (size) of the prostate gland with transrectal ultrasound (discussed below) and divides the PSA number by the prostate volume. A higher PSA density (PSAD)

indicates greater likelihood of cancer. PSA density has not been shown to be that useful. The percent-free PSA test has so far been shown to be more accurate.

### **Age-specific PSA Ranges**

A PSA result within the borderline range might be very worrisome in a 50-year-old man but cause less concern in an 80-year-old man. It is known that PSA levels are normally higher in older men than in younger men, even when there is no cancer. For this reason, some doctors have suggested comparing PSA results with results from other men of the same age.

But because the usefulness of age-specific PSA ranges is not well proven, most doctors and professional organizations (as well as the makers of the PSA tests) do not recommend their use at this time.

### **Use of the PSA Blood Test After Prostate Cancer Diagnosis**

Although the PSA test is used mainly to detect prostate cancer early, it is useful in other situations:

- In men diagnosed with prostate cancer, the PSA test can be used together with clinical exam results and tumor grade (from the biopsy) to help decide if further tests (such as CT scans or bone scans) are needed.
- It can help tell whether your cancer is still confined to the prostate gland. If your PSA level is very high, your cancer has likely spread beyond the prostate. This may affect your treatment options, since some forms of therapy (such as surgery and radiation) are not likely to be helpful if the cancer has spread to the lymph nodes, bones, or other organs.
- After surgery or radiation treatment, the PSA level can be watched to help determine if the treatment was successful. PSA levels normally fall to very low levels if the treatment removed or destroyed all of the prostate cells. A rising PSA level (especially after surgery) likely means that prostate cancer cells are present and your cancer has come back.
- If you choose a "watchful waiting" approach to treatment, the PSA level can be used to help decide whether the cancer is growing and if active treatment should be considered.
- During hormonal therapy or chemotherapy, the PSA level can help indicate how well the treatment is working or when it may be time to try a different form of treatment.

If prostate cancer has come back (recurred) after treatment, or if it has spread outside of the prostate (metastatic disease), the actual PSA number is probably not as important as whether it changes. The PSA number does not predict whether or not a person will have symptoms or how long he will live. Many people have very high PSA values and feel just fine. Other people have low values and have symptoms. With advanced disease, it may be more important to look at the way the PSA level is changing rather than the actual number.

## **Digital Rectal Exam (DRE)**

During this exam, a doctor inserts a gloved, lubricated finger into the rectum to feel for any bumps or hard areas that might be a cancer. The prostate gland is found just in front of the rectum, and most cancers begin in the back part of the gland, which can be felt during a rectal exam. While it is uncomfortable, the exam causes no pain and only takes a short time.

Although DRE is less effective than the PSA blood test in finding prostate cancer, it can sometimes find cancers in men with normal PSA levels. For this reason, the American Cancer Society guidelines recommend that when prostate cancer screening is done, both the DRE and PSA blood test should be used.

The DRE can also be used once a man is known to have prostate cancer to try to determine if it may have spread to nearby tissues and to detect cancer that has come back after treatment.

## **Transrectal Ultrasound (TRUS)**

Transrectal ultrasound (TRUS) uses sound waves to make an image of the prostate on a video screen. For this test, a small probe is placed in the rectum. It gives off sound waves, which enter the prostate and create echoes that are picked up by the probe. A computer turns the pattern of echoes into a black and white image of the prostate.

The procedure takes only a few minutes and is done in a doctor's office or outpatient clinic. You will feel some pressure when the TRUS probe is placed in your rectum, but it is usually not painful.

TRUS is usually not recommended as a routine test by itself to detect prostate cancer because it doesn't often show early cancer. Instead, it is most commonly used during a prostate biopsy (described in the next section). TRUS is used to guide the biopsy needles into the right area of the prostate.

TRUS is useful in other situations as well. It can be used to measure the size of the prostate gland, which can help determine the PSA density and may also affect which treatment options a man has. It is also used as a guide during some forms of treatment such as cryosurgery.

## **Signs and Symptoms of Prostate Cancer**

Early prostate cancer usually causes no symptoms and is most often found by a PSA test and/or DRE. Some advanced prostate cancers can slow or weaken your urinary stream or make you need to urinate more often. But non-cancerous diseases of the prostate, such as BPH (benign prostatic hyperplasia) cause these symptoms more often.

If the prostate cancer is advanced, you might have blood in your urine (hematuria) or trouble getting an erection (impotence). Advanced prostate cancer commonly spreads to the bones, which can cause pain in the hips, spine, ribs, or other areas. Cancer that has spread to the

spine can also press on the spinal nerves, which can result in weakness or numbness in the legs or feet, or even loss of bladder or bowel control.

Other diseases, however, can also cause many of these same symptoms. It is important to tell your doctor if you have any of these problems so that the cause can be found and treated.

## How Is Prostate Cancer Diagnosed?

If certain symptoms or the results of early detection tests -- the prostate-specific antigen (PSA) blood test and/or digital rectal exam (DRE) -- suggest that you might have prostate cancer, your doctor will do a prostate biopsy to find out if the disease is present.

### The Prostate Biopsy

A biopsy is a procedure in which a sample of body tissue is removed and then looked at under a microscope. A *core needle biopsy* is the main method used to diagnose prostate cancer. It is usually done by a urologist, a surgeon who treats cancers of the genital and urinary tract, which includes the prostate gland. Using transrectal ultrasound (described in the section, "Can Prostate Cancer Be Found Early?") to "see" the prostate gland, the doctor quickly inserts a needle through the wall of the rectum into the prostate gland. When pulled out, the needle removes a small cylinder of tissue, usually about 1/2-inch long and 1/16-inch across. This is repeated from 8 to 18 times, although most urologists will take about 12 samples. These are sent to the lab to see if cancer is present.

Though the procedure sounds painful, it typically causes only a very brief, uncomfortable sensation because it is done with a special spring-loaded biopsy instrument. The device inserts and removes the needles in a fraction of a second. Most doctors who do the biopsy will numb the area first with local anesthetic. You might want to ask your doctor if he or she plans to do this.

Some doctors will do the biopsy through the perineum, the skin between the rectum and the scrotum. The doctor will place his or her finger in your rectum to feel the prostate and then insert the biopsy needle through a small incision in the skin of the perineum. The doctor will also use a local anesthetic to numb the area.

The biopsy itself takes about 15 minutes and is usually done in the doctor's office. You will likely be given antibiotics to take before the biopsy and for a day or 2 after to reduce the risk of infection.

For a few days after the procedure, you may feel some soreness in the area and will likely notice blood in your urine. You may also have some light bleeding from your rectum. Many men also see some blood in their semen, which can last for several weeks after the biopsy.

Your biopsy samples will be sent to a pathology lab. There, a *pathologist* (a doctor who specializes in diagnosing disease in tissue samples) will see if there are cancer cells in your biopsy by looking at the samples under the microscope. If cancer is present, the pathologist

will also assign it a *grade* (see below). Getting the results usually takes 1 to 3 days, but it can take longer.

Even with many samples, biopsies can still sometimes miss a cancer if none of the biopsy needles pass through it. This is known as a "false negative" result. If your doctor still strongly suspects prostate cancer (due to a very high PSA level, for example) a repeat biopsy may be needed to help be sure.

## Grading the Prostate Cancer

Almost all pathologists grade prostate cancers according to the Gleason system. This system assigns a Gleason grade, using numbers from 1 to 5 based on how much the cells in the cancerous tissue look like normal prostate tissue.

- If the cancerous tissue looks much like normal prostate tissue, a grade of 1 is assigned.
- If the cancer lacks these normal features and its cells seem to be spread haphazardly through the prostate, it is called a grade 5 tumor.
- Grades 2 through 4 have features in between these extremes.

Because prostate cancers often have areas with different grades, a grade is assigned to the 2 areas that make up most of the cancer. These 2 grades are added together to yield the *Gleason score* (also called the Gleason sum) between 2 and 10. The higher your Gleason score, the more likely it is that your cancer will grow and spread quickly.

## Other Elements of a Biopsy Report

Aside from the grade of the cancer (if it is present), the pathologist's report often contains other pieces of information that may give a better idea of the scope of the cancer. These can include:

- the number of biopsy core samples that contain cancer (for example, "7 out of 12")
- the percentage of cancer in each of the cores
- whether the cancer is on one side (left or right) or both sides of the prostate

## "Suspicious" Results

Sometimes when the pathologist looks at the prostate cells under the microscope, they don't look cancerous, but they're not quite normal, either. These results are often reported as "suspicious." They generally fall into 2 categories -- either "prostatic intraepithelial neoplasia" (PIN) or "atypical small acinar proliferation" (ASAP).

In PIN, there are changes in how the prostate cells look under the microscope, but the cells are basically still in place -- they don't look like they've invaded into other parts of the prostate (like cancer cells would). PIN is often divided into low-grade and-high grade. Many



men begin to develop low-grade PIN at an early age and do not necessarily develop prostate cancer. The importance of low-grade PIN in relation to prostate cancer is still unclear.

If high-grade PIN is found on a biopsy, there is about a 20% chance that cancer may already be present somewhere else in the prostate gland. For this reason, doctors often watch men with high-grade PIN carefully and may advise a repeat prostate biopsy, especially if the original biopsy did not take samples from all parts of the prostate.

Another finding that is sometimes reported on a prostate biopsy is *atypical small acinar proliferation (ASAP)*, which is sometimes just called *atypia*. In ASAP, the cells look like they might be cancerous when viewed under the microscope, but there are too few of them to be sure. If ASAP is found, there's about a 40% to 50% chance that cancer is also present in the prostate, which is why many doctors recommend getting a repeat biopsy within a few months.

## How Is Prostate Cancer Staged?

The stage (extent) of a cancer is one of the most important factors in choosing treatment options and predicting a patient's outlook for survival. If your prostate biopsy confirms that you have cancer, more tests may be done to find out how far it has spread within the prostate, to nearby tissues, or to other parts of the body. This process is called staging.

Your doctor will use your digital rectal exam (DRE) results, prostate-specific antigen (PSA) level, and Gleason score to figure out how likely it is that your cancer has spread outside of the prostate. This information is used to decide which other tests (if any) need to be done before deciding on a treatment. Men with a normal DRE result, a low PSA, and a low Gleason score may not need any other tests because the chance that the cancer has spread is so low.

## Medical History and Physical Exam

The physical exam, especially the DRE, is an important part of prostate cancer staging. By doing a DRE your doctor can sometimes tell whether the cancer is only on one side of the prostate, whether it is present on both sides, or whether it is likely to have spread beyond the prostate gland to nearby tissues. The DRE is always used together with the PSA blood test for early detection of prostate cancer and is discussed in the section, "Can Prostate Cancer Be Found Early?" Your doctor may also examine other areas of your body to see whether the cancer has spread.

Your doctor will also ask you about symptoms such as urinary problems or bone pain, which could suggest that the cancer may have spread to your bones.

## Imaging Tests Used for Prostate Cancer Staging

Not all men with prostate cancer need to have imaging tests, but for those who do, the following tests are sometimes used.

### Radionuclide "Bone Scan"

When prostate cancer spreads to distant sites, it often goes to the bones first. (Even when prostate cancer spreads to the bone, it is still called prostate cancer, not bone cancer.) A bone scan can help show whether cancer has reached the bones.

For this test, a small amount of low-level radioactive material is injected into a vein (intravenously, or IV). The substance settles in damaged bone tissue throughout the entire skeleton over the course of a couple of hours. You then lie on a table for about 30 minutes while a special camera detects the radioactivity and creates a picture of your skeleton.

Areas of bone damage appear as "hot spots" on your skeleton -- that is, they attract the radioactivity. These areas may suggest the presence of metastatic cancer, but arthritis or other bone diseases can also cause the same pattern. To distinguish between these conditions, your cancer care team may use other imaging tests such as simple x-rays or CT or MRI scans to get a better look at the areas that light up, or they may even take biopsy samples of the bone.

The injection itself is the only uncomfortable part of the scanning procedure. The radioactive material is passed out of the body in the urine over the next few days. Because the amount of radioactivity used is very low, it carries very little risk to you or others, but you may want to ask your doctor if you should take any special precautions after having this test.

### **Computed Tomography (CT)**

The CT scan (also known as a CAT scan) is a special kind of x-ray that gives detailed, cross-sectional images of your body. Instead of taking one picture, like a standard x-ray, a CT scanner takes many pictures of the part of your body being studied as it rotates around you. A computer then combines these pictures into images of slices of the part of your body being studied.

After the first set of pictures is taken you may be asked to drink 1 or 2 pints of a radiocontrast agent, or "dye." You may also receive an IV (intravenous) line through which the contrast dye is injected. This helps better outline structures in your body. You will also need to drink enough liquid to have a full bladder. This will keep the bowel away from the area of the prostate gland. A second set of pictures is then taken.

The solution you drink and the injection may cause some flushing (a feeling of warmth, especially in the face). Some people are allergic and get hives. Rarely, more serious reactions like trouble breathing or low blood pressure can occur. Be sure to tell the doctor if you have ever had a reaction to any contrast material used for x-rays.

CT scans take longer than regular x-rays. You need to lie still on a table while they are being done. During the test, the table moves in and out of the scanner, a ring-shaped machine that completely surrounds the table. You might feel a bit confined by the ring you have to lie in while the pictures are being taken.

This test can help tell whether prostate cancer has spread into nearby lymph nodes. If your prostate cancer has come back after treatment, the CT scan can often tell whether it is

growing into other organs or structures in your pelvis. On the other hand, CT scans rarely provide useful information about newly diagnosed prostate cancers that are likely to be confined to the prostate based on other findings (DRE result, PSA level, and Gleason score). CT scans are not as useful as magnetic resonance imaging (MRI) for looking at the prostate gland itself.

### **Magnetic Resonance Imaging (MRI)**

MRI scans use radio waves and strong magnets instead of x-rays. The energy from the radio waves is absorbed by the body and then released in a pattern formed by the type of body tissue and by certain diseases. A computer translates the pattern into a very detailed image of parts of the body. This produces cross-sectional slices of the body like a CT scanner, but it can also show slices (views) from several angles. As with CT scans, a contrast material might be injected, but this is done less often.

MRI scans can be very helpful in looking at prostate cancer. They can produce a very clear picture of the prostate and show whether the cancer has spread outside the prostate into the seminal vesicles or the bladder. This information can be very important for your doctors in planning your treatment. But like CT scans, they may not provide useful information about newly diagnosed prostate cancers that are likely to be localized (confined to the prostate) based on other factors.

MRI scans take longer than CT scans -- often up to an hour. During the scan, you need to lie still inside a narrow tube, which is confining and can upset people who don't like enclosed spaces. The machine also makes clicking and buzzing noises. Some places provide headphones with music to block this out. To improve the accuracy of the MRI, many doctors will place a probe, called an endorectal coil, inside your rectum. This must stay in place for 30 to 45 minutes and can be uncomfortable.

### **ProstaScint™ Scan**

Like the bone scan, the ProstaScint scan uses an injection of low-level radioactive material to find cancer that has spread beyond the prostate. Both tests look for areas of the body where the radioactive material collects, but they work in different ways.

While the radioactive material used for the bone scan is attracted to bone, the material for the ProstaScint scan is attracted to prostate cells in the body. It is attached to a monoclonal antibody, a type of man-made protein that recognizes and sticks to a particular substance. In this case, the antibody sticks to prostate-specific membrane antigen (PSMA), a substance found at high levels in normal and cancerous prostate cells.

After the material is injected, you will be asked to lie on a table while a special camera creates an image of the body. This is usually done about half an hour after the injection and again 3 to 5 days later.

The advantage of this test is that it can find prostate cancer cells in lymph nodes and other soft (non-bone) organs and can help pick out prostate cancer from other cancers or benign problems. But the test is not always accurate, and the results can sometimes be confusing.

Most doctors do not recommend this test for men who have just been diagnosed with prostate cancer. But it may be useful if your blood PSA level begins to rise after treatment and other tests are not able to find the exact location of your cancer. Doctors may not order this test if they believe it will not be helpful for a given patient.

## **Lymph Node Biopsy**

A lymph node biopsy (also called a lymph node dissection or lymphadenectomy) is sometimes done to find out whether the cancer has spread from the prostate to nearby lymph nodes. If cancer cells are found in the lymph node biopsy specimen, surgery to cure the cancer is usually not done and other treatment options are considered. Lymph node biopsies are rarely done unless your doctor is concerned that the cancer has spread. There are several ways to biopsy lymph nodes.

### **Surgical Biopsy**

The surgeon may remove lymph nodes through an incision in the lower part of your abdomen. This is often done in the same operation as the radical prostatectomy (see the section, "How Is Prostate Cancer Treated?" for information about radical prostatectomy).

If the surgeon has a reason to suspect that the cancer may have spread (such as a PSA level over 20 or a Gleason score over 7), he or she may remove the nodes before attempting to remove the prostate gland. A pathologist then looks at the nodes while you are still under anesthesia to help the surgeon decide whether to continue with the radical prostatectomy. This is called a *frozen section* exam, because the tissue sample is frozen before thin slices are taken to check under a microscope. If the nodes contain cancer, the operation is usually stopped. This is because removing the prostate would be unlikely to cure the cancer, and it could still result in serious complications or side effects.

If the likelihood of spread is low, most surgeons do not request a frozen section exam and instead send the lymph nodes to be looked at along with the removed prostate gland. The test results are usually available 3 to 7 days after surgery.

### **Laparoscopy**

A surgeon may use a laparoscope (a long, slender tube with a small video camera on the end), which is inserted into the abdomen through a very small incision. Other small incisions are made to insert long instruments to remove the lymph nodes. The surgeon removes all of the lymph nodes around the prostate gland and sends them to the pathologist. Because there are no large incisions, most people recover fully in only 1 or 2 days, and the operation leaves very small scars. This procedure is not common, but it is sometimes used when it's important to know the lymph node status and radical prostatectomy is not planned (such as for certain men who choose treatment with radiation therapy).

## **Fine Needle Aspiration (FNA)**

If your lymph nodes appear enlarged on an imaging study (CT or MRI) a specially trained radiologist may take a sample of cells from an enlarged lymph node by using a technique called fine needle aspiration (FNA). To do this, the doctor uses the CT scan image to guide a long, thin needle through the skin in the lower abdomen and into an enlarged lymph node. A syringe attached to the needle allows the doctor to take a small tissue sample from the node. Before the needle is placed, your skin will be numbed with local anesthesia. You will be able to return home a few hours after the procedure. This method is not used very often.

## **The AJCC TNM Staging System**

A staging system is a standard way in which the cancer care team describes the extent to which a cancer has spread. While there are several different staging systems for prostate cancer, the most widely used system is the American Joint Committee on Cancer (AJCC) TNM System.

The TNM System describes:

- the extent of the primary *tumor* (T category)
- whether the cancer has spread to nearby lymph *nodes* (N category)
- the absence or presence of distant *metastasis* (M category)

The overall stage takes all 3 categories into account, along with the Gleason score (described in the section, "How Is Prostate Cancer Diagnosed?").

There are actually 2 types of staging for prostate cancer. The *clinical stage* is your doctor's best estimate of the extent of your disease, based on the results of the physical exam (including DRE), lab tests, prostate biopsy, and any imaging studies you have had.

If you have surgery, your doctors can also determine the *pathologic stage*, which is based on the surgery and examination of the removed tissue. This means that if you have surgery, the stage of your cancer might actually change afterward (if cancer was found in a place it wasn't suspected, for example). Pathologic staging is likely to be more accurate than clinical staging, as it allows your doctor to get a firsthand impression of the extent of your disease. This is one possible advantage of having surgery (radical prostatectomy) as opposed to radiation therapy or watchful waiting (expectant management).

Both types of staging use the same categories (although the T1 category is not used in pathologic staging).

### **T Categories**

There are 4 categories for describing the local extent of the prostate tumor, ranging from T1 to T4. Most of these have subcategories as well.

**T1:** Your doctor can't feel the tumor or see it with imaging such as transrectal ultrasound.

**T1a:** The cancer is found incidentally during a transurethral resection of the prostate (often abbreviated as TURP) that was done for benign prostatic hyperplasia (BPH). Cancer is present in less than 5% of the tissue removed.

**T1b:** The cancer is found during a TURP but is present in more than 5% of the tissue removed.

**T1c:** The cancer is found by needle biopsy that was done because of an increased PSA.

**T2:** Your doctor can feel the cancer when a digital rectal exam (DRE) is done, but it still appears to be confined to the prostate gland.

**T2a:** The cancer is in one half or less of only one side (left or right) of your prostate.

**T2b:** The cancer is in more than half of only one side (left or right) of your prostate.

**T2c:** The cancer is in both sides of your prostate.

**T3:** The cancer has begun to spread outside your prostate and may involve the seminal vesicles.

**T3a:** The cancer extends outside the prostate but not to the seminal vesicles.

**T3b:** The cancer has spread to the seminal vesicles.

**T4:** The cancer has spread to tissues next to your prostate (other than the seminal vesicles), such as the bladder sphincter (muscle that helps control urination), the rectum, and/or the wall of the pelvis.

### **N Categories**

**N0:** The cancer has not spread to any lymph nodes.

**N1:** The cancer has spread to one or more regional (nearby) lymph nodes in the pelvis.

### **M Categories**

**M0:** The cancer has not spread beyond the regional lymph nodes.

**M1:** The cancer has spread beyond the regional nodes.

**M1a:** The cancer has spread to distant (outside of the pelvis) lymph nodes.

**M1b:** The cancer has spread to the bones.

**M1c:** The cancer has spread to other organs such as lungs, liver, or brain (with or without bone disease).

### **Stage Groupings**

Once the T, N, and M categories have been determined, this information is combined, along with the Gleason score, in a process called stage grouping. The overall stage is expressed in Roman numerals from I (the least advanced) to IV (the most advanced). This is done to help determine treatment options and the outlook for survival or cure.

#### **Stage I: T1a, N0, M0, low Gleason score (2 to 4)**

The cancer is still within the prostate and has not spread to lymph nodes or elsewhere in the body. The cancer was found during a transurethral resection, it had a low Gleason score (2 to 4), and less than 5% of the tissue was cancerous.

**Stage II: T1a, N0, M0, Gleason score of 5 to 10; OR T1b-T2, N0, M0, any Gleason score**  
The cancer is still within the prostate and has not spread to the lymph nodes or elsewhere in the body, and one of the following applies:

- It was found during a transurethral resection and has an intermediate or high Gleason score (5 or higher), or more than 5% of the tissue contained cancer; or
- It was discovered because of a high PSA level, cannot be felt on digital rectal exam or seen on transrectal ultrasound, and was diagnosed by needle biopsy; or
- It can be felt on digital rectal exam or seen on transrectal ultrasound.

**Stage III: T3, N0, M0, any Gleason score (2 to 10)**

The cancer has begun to spread outside the prostate and may have spread to the seminal vesicles, but it has not spread to the lymph nodes or elsewhere in the body.

**Stage IV: T4, N0, M0; OR any T, N1, M0; OR any T, any N, M1 (any Gleason score)**

One or more of the following apply:

- The cancer has spread to tissues next to the prostate (other than the seminal vesicles), such as the bladder's external sphincter (muscle that helps control urination), rectum, and/or the wall of the pelvis; and/or
- It has spread to the lymph nodes; and/or
- It has spread to other, more distant sites in the body.

In addition to the TNM system, other systems have been used to stage prostate cancer. The Whitmore-Jewett system, which stages prostate cancer as A, B, C, or D, was commonly used in the past, but most prostate specialists now use the TNM system. If your doctors use this system, ask them to translate it into the TNM system or to explain how their staging will determine your treatment options.

## How Is Prostate Cancer Treated?

*This information represents the views of the doctors and nurses serving on the American Cancer Society's Cancer Information Database Editorial Board. These views are based on their interpretation of studies published in medical journals, as well as their own professional experience.*

*The treatment information in this document is not official policy of the Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor.*

*Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.*

This section starts with general comments about the types of treatments used for prostate cancer. This is followed by a discussion of the typical treatment options based on the stage of the cancer.

## Some General Comments About Treatment

Once your prostate cancer has been diagnosed, graded, and staged, you have a lot to think about before you and your doctor choose a treatment plan. You may feel that you must make a decision quickly, but it is important to give yourself time to absorb the information you have just learned. Ask questions of your cancer care team. Read the section, "What Should You Ask Your Doctor About Prostate Cancer?"

The treatment you choose for prostate cancer should take into account:

- your age and expected life span
- any other serious health conditions you may have
- the stage and grade of your cancer
- your feelings (and your doctor's opinion) about the need to treat the cancer
- the likelihood that each type of treatment will cure your cancer (or provide some other measure of benefit)
- your feelings about the side effects common with each treatment

You may want to get a second opinion about the best treatment option for your situation, especially if there are several choices available to you. Prostate cancer is a complex disease, and doctors may differ in their opinions regarding the best treatment options. Speaking with doctors who specialize in different kinds of treatment may be helpful. You will want to weigh the benefits of each treatment against its possible outcomes, side effects, and risks.

### **Expectant Management (Watchful Waiting)**

Because prostate cancer often grows very slowly, some men (especially those who are older or have other serious health problems) may never need treatment for their prostate cancer. Instead, their doctors may recommend an approach known as expectant management, or "watchful waiting." This approach involves closely monitoring the cancer without active treatment such as surgery or radiation therapy. It may be recommended if your cancer is not causing any symptoms, is expected to grow very slowly, and is small and contained within one area of the prostate.

Watchful waiting is less likely to be a good option if you are young, healthy, and/or have a fast-growing cancer (for example, a high Gleason score).

At this time, watchful waiting is a reasonable option for some men with slow-growing cancers because it is not known whether active treatment such as surgery, radiation therapy, and hormone therapy (described below), prolongs survival. On the other hand, active treatment carries definite risks and side effects that may sometimes outweigh the possible benefits. Some men choose watchful waiting for this reason. Others are not comfortable with this approach, and are willing to accept the possible side effects of active treatments in order to try to remove or destroy the cancer.

Watchful waiting does not mean that you will not receive medical care or follow-up. Rather, your cancer will be carefully monitored. Usually this approach includes a PSA blood test and digital rectal examination (DRE) every 3 to 6 months or so, possibly with yearly transrectal ultrasound-guided biopsy of the prostate. If you develop bothersome symptoms or your



cancer begins to grow more quickly, you can consider active treatment. A possible downside of this approach is that there's a chance it could allow the cancer to become more advanced, which might limit treatment options.

Hopefully we will have a better idea of the pros and cons of watchful waiting versus active treatment in the near future. A large study sponsored by the National Cancer Institute and the Veterans Affairs Cooperative Studies Program is now looking into how active treatment affects survival and quality of life of prostate cancer patients of different ages. The PIVOT (short for Prostatic Intervention Versus Observation Trial) is still in progress.

## **Surgery**

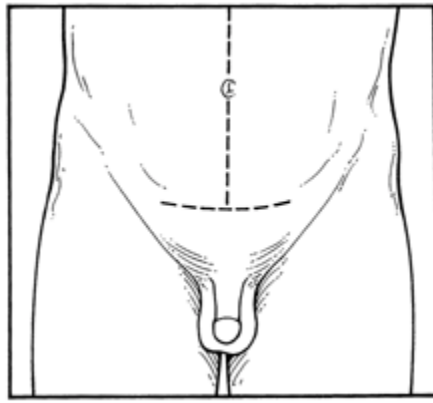
Radical prostatectomy is surgery that attempts to cure prostate cancer. It is used most often if the cancer is not thought to have spread outside of the gland (stage T1 or T2 cancers). In this operation, your surgeon is trying to cure you by removing the entire prostate gland plus some of the tissue around it, including the seminal vesicles.

### **Radical Retropubic Prostatectomy**

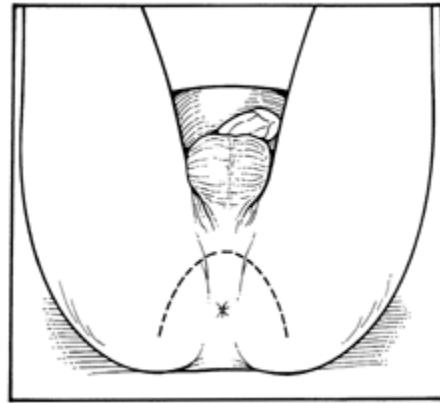
This is the operation used by most urologic surgeons (urologists). You will be either under general anesthesia (asleep) or be given spinal or epidural anesthesia (numbing the lower half of the body) along with sedation during the surgery.

For this operation, the surgeon makes a skin incision in your lower abdomen, from the belly button down to the pubic bone. If there is a reasonable chance the cancer may have spread to the lymph nodes (based on your PSA level, DRE, and biopsy results), the surgeon may remove lymph nodes from around the prostate at this time. If any of the nodes contain cancer cells, which means the cancer has spread, they often will not continue with the surgery because it is unlikely that the cancer can be cured.

The surgeon will pay close attention to the 2 tiny bundles of nerves that run on either side of the prostate. These nerves control erections. If you are able to have erections before surgery, the surgeon will try not to injure these nerves (known as a "nerve-sparing" approach). If the cancer is growing into or very close to the nerves the surgeon will need to remove them. If they are both removed, you will be impotent (unable to have a spontaneous erection). This means that you will need help (such as medications or pumps) to have erections. If the nerves on one side are removed, you still have a chance of keeping your ability to have an erection, but it is lower than if neither were removed. If neither nerve bundle is removed you may be able to function normally. Usually it takes at least a few months after surgery to have an erection because the nerves have been handled during the operation and won't work properly for a while.



Retropubic approach



Perineal approach

### **Radical Perineal Prostatectomy**

In this operation, the surgeon makes the incision in the skin between the anus and scrotum (the perineum), as shown in the picture above. This approach is used less often because the nerves cannot easily be spared and lymph nodes can't be removed. But it is often a shorter operation and might be an option if you don't want the nerve-sparing procedure or require lymph node removal. It also might be used if you have other medical conditions that make retropubic surgery difficult for you. It can be just as curative as the retropubic operation if done correctly.

These operations usually last from 1 1/2 to 4 hours. The perineal operation usually takes less time than the retropubic operation, and may result in less pain afterward. After surgery you will stay in the hospital for about 3 days and will probably be away from work for about 3 to 5 weeks.

In most cases, you will be able to donate your own blood before surgery. If needed, this blood can be given back to you during the operation.

After the surgery, while you are still under anesthesia, a catheter will be put in your penis to help drain your bladder. The catheter usually stays in place for 1 to 3 weeks while you are healing. You will be able to urinate on your own after the catheter is removed.

### **Laparoscopic Radical Prostatectomy (LRP)**

Both of the surgical approaches above use an "open" technique, in which the surgeon makes a long incision to remove the prostate. A newer technique, known as laparoscopic radical prostatectomy (LRP), uses several smaller incisions, through which special long instruments are inserted to remove the prostate. One of the instruments has a small video camera on the end, which allows the surgeon to see inside the abdomen.

Laparoscopic prostatectomy has some advantages over the usual open radical prostatectomy, including less blood loss and pain, shorter hospital stays (usually no more than a day), and faster recovery times (although the catheter will be needed for about the same amount of

time). LRP offers very good lighting and magnification, which can help the surgeon better decide which areas need to be removed.

Still, LRP is a challenging operation for surgeons to learn, and usually requires a bit more time on the operating table (and under anesthesia). Another possible drawback is that it does not allow the surgeon to use the sense of touch while operating or to have the same freedom of motion that his or her hands would have.

LRP has been used in the United States since 1999 and is more frequently being done both in community and university centers. In experienced hands, LRP appears to be as good as open radical prostatectomy, although we do not yet have long-term results from procedures done in the United States. Early studies report that the rates of side effects from LRP seem to be about the same as for open prostatectomy. A nerve-sparing approach is possible with LRP, increasing the chance of normal erections after the operation.

### **Robotic-assisted Laparoscopic Radical Prostatectomy**

An even newer approach is to do LRP remotely using a robotic interface (called the da Vinci system). The surgeon sits at a panel near the operating table and controls robotic arms to perform the operation through several small incisions in the patient's abdomen. For the patient, there is little difference between direct and remote (robotic) LRP, either during surgery or recovery.

For the surgeon, the robotic system may provide more maneuverability and more precision when moving the instruments than standard LRP. But the most important factor in the success of either type of LRP is the surgeon's experience, commitment, and skill.

Robotic LRP has been in use for only a few years in the United States. The machines themselves are expensive, and are available in only a limited number of medical centers across the country. Still, this approach has become more popular in recent years. Early reports have found less blood loss and shorter recovery times compared to standard radical prostatectomy. But because it is still a relatively new way of doing the surgery, reports of long-term outcomes are not yet available.

If you are thinking about treatment with either type of LRP, it's important to understand what is known and what is not yet known about this approach. Again, the most important factors are likely to be the skill and experience of your surgeon. If you decide that LRP is the treatment for you, be sure to find a surgeon with a lot of experience doing LRP.

### **Transurethral Resection of the Prostate (TURP)**

This operation is palliative, which means it is done to relieve symptoms, not to cure. This surgery may be used if you are having trouble urinating because of the cancer. More often, TURP is used to treat men with non-cancerous enlargement of the prostate called benign prostatic hyperplasia (BPH).

During this operation, the surgeon removes the inner part of the prostate gland that surrounds the urethra (the tube through which urine exits the bladder). The skin is not cut with this surgery. An instrument called a resectoscope is passed through the end of the penis into the urethra to the level of the prostate. Once it is in place, electricity is passed through a wire to heat it and cut or vaporize the tissue. Either spinal anesthesia (which numbs the lower half of your body) or general anesthesia (where you are asleep) is used.

The operation usually takes about an hour. After surgery, a catheter is inserted through the penis into the bladder. It remains in place for 1 to 3 days to help urine drain while the prostate heals. You can usually leave the hospital after 1 to 2 days and return to work in 1 to 2 weeks. You will likely have some blood in your urine after surgery. Other side effects from TURP include infection and the risks that come with the type of anesthesia that was used.

### **Surgical Risks and Possible Side Effects of Radical Prostatectomy (Including LRP)**

There are possible risks and side effects with any type of surgery for prostate cancer.

**Surgical risks:** The risks with any type of radical prostatectomy are much like those of any major surgery, including risks from anesthesia. Among the most serious, there is a small risk of heart attack, stroke, blood clots in the legs that may travel to your lungs, and infection at the incision site. Because there are many blood vessels near the prostate gland, another risk is bleeding during and after the surgery. You may need blood transfusions, which carry their own small risk. In extremely rare cases, people die because of complications of this operation. Your risk depends, in part, on your overall health, your age, and the skill of your surgical team.

The major possible *side effects* of radical prostatectomy are urinary incontinence (being unable to control urine) and impotence (being unable to have erections). It should be noted that these side effects are also possible with other forms of therapy, although they are described here in more detail.

**Urinary incontinence:** You may develop urinary incontinence, which means you can't control your urine or have leakage or dribbling. There are different degrees of incontinence. Being incontinent can affect you not only physically but emotionally and socially as well.

There are 3 types of incontinence:

- stress incontinence
- overflow incontinence
- urge incontinence

Men with *stress incontinence* leak urine when they cough, laugh, sneeze, or exercise. It is usually caused by problems with the muscular valve that keeps urine in the bladder (the bladder sphincter). Prostate cancer treatments may damage the muscles that form this valve or the nerves that keep the muscles working. Stress incontinence is the most common type of incontinence after prostate surgery.

Men with *overflow incontinence* take a long time to urinate and have a dribbling stream with little force. Overflow incontinence is usually caused by blockage or narrowing of the bladder outlet by cancer or scar tissue.

Men with *urge incontinence* have a sudden need to go to the bathroom and pass urine. This problem occurs when the bladder becomes too sensitive to stretching as urine fills it.

For men who have had surgery for prostate cancer, normal bladder control usually returns within several weeks or months after radical prostatectomy. This recovery usually occurs gradually, in stages.

Doctors can't predict how any man will function after surgery. In one study of 901 men aged 55 to 74 who were treated in all different types of hospitals, researchers found that 5 years after radical prostatectomy:

- 15% of the 901 men had no bladder control or had frequent leaks or dripping of urine
- 16% leaked at least twice a day
- 29% wore pads to keep dry (Some of the men were in 2 or 3 of these groups, so adding these percentages together overstates the likelihood of urinary problems.)

Most large cancer centers, where prostate surgery is done more often and surgeons have more experience, report fewer problems with incontinence.

Treatment of incontinence depends on its type, cause, and severity. If you have problems with incontinence, let your doctors know. You might feel embarrassed about discussing this issue, but remember that you are not alone. This is a common problem. Doctors who treat men with prostate cancer should know about incontinence and be able to suggest ways to improve it.

Your doctor may recommend special exercises, called *Kegel exercises*, to help strengthen your bladder muscles. These exercises involve tensing and relaxing certain pelvic muscles. Not all doctors agree about their usefulness or the best way to do them, so ask your doctor about doing Kegels before you try them.

There are also *medicines* to help the muscles of the bladder or sphincter. Most of these medicines affect either the muscles or the nerves that control them. These medicines are more effective for some forms of incontinence than for others.

*Surgery* may also be used to correct long-term incontinence. Material such as collagen can be injected to tighten the bladder sphincter. If your incontinence is severe and not getting better on its own, an artificial sphincter can be implanted, or a small device called a urethral sling may be implanted to keep the bladder neck where it belongs. Ask your doctor if these treatments might help you.

If your incontinence cannot be completely corrected, it can still be helped. You can learn how to manage and live with your incontinence. Incontinence is more than a physical problem. It can disrupt your quality of life if it is not managed well.

There is no one right way to cope with incontinence. The challenge is to find what works for you so that you can return to your normal daily activities. There are many *incontinence products* to help keep you mobile and comfortable, such as pads that are worn under your clothing. Adult briefs and undergarments are bulkier than pads but provide more protection. Bed pads or absorbent mattress covers can also be used to protect the bed linens and mattress.

When choosing incontinence products, keep in mind the checklist below. Some of these questions may not be important to you, or you may have others to add.

**Absorbency:** How much does the product provide? How long will it protect?

**Bulk:** Can it be seen under normal clothing? Is it disposable? Or reusable?

**Comfort:** How does it feel when you move or sit down?

**Availability:** Which stores carry the product? Are they easy to get to?

**Cost:** Does your insurance pay for these products?

Another option is a rubber sheath called a condom catheter that can be put over the penis to collect urine in a bag. There are also compression (pressure) devices that can be placed on the penis for short periods of time to keep urine from coming out.

For some types of incontinence, self-catheterization may be an option. In this approach, you insert a thin tube into your urethra to drain and empty the bladder. Most people can learn this safe and usually painless technique.

You can also follow some simple precautions that may make incontinence less of a problem. For example, empty your bladder before bedtime or before strenuous activity. Avoid drinking too much fluid, particularly if the drinks contain caffeine or alcohol, which can make you have to go more often. Because fat in the abdomen can push on the bladder, losing weight sometimes helps improve bladder control.

Fear, anxiety, and anger are common feelings for people dealing with incontinence. Fear of having an accident may keep you from doing the things you enjoy most -- taking your grandchild to the park, going to the movies, or playing a round of golf. You may feel isolated and embarrassed. You may even avoid sex because you are afraid of leakage. Be sure and talk to your doctor so you can begin to manage this problem.

**Impotence:** Impotence, also known as erectile dysfunction, means you cannot get an erection sufficient for sexual penetration. The nerves that allow men to get erections may be damaged or removed by radical prostatectomy. Other treatments may also damage these nerves or the blood vessels that supply blood to the penis to cause an erection.

Recovery of sexual function can take up to 2 years after surgery. During the first several months, you will probably not be able to have a spontaneous erection, so you may need to use medicines or other treatments. Your ability to have an erection after surgery will be related to your age, your ability to get an erection before the operation, and whether the nerves were cut. You should expect some decrease in your ability to have an erection, but the younger you are, the more likely it is that you will keep this ability.

There is a wide range of impotency rates reported in the medical literature. Some cancer centers that perform many radical *nerve-sparing* prostatectomies report impotence rates as low as 25% to 30% for men under 60, and as low as 10% for men under 50. However, other doctors have reported higher rates of impotence in similar patients. Impotence occurs in about 70% to 80% of men over 70, even if nerves on both sides are not removed.

If potency remains after surgery, the sensation of orgasm should continue to be pleasurable, but there is no ejaculation of semen -- the orgasm is "dry." This is because during the prostatectomy, the glands that made most of the fluid for semen (the seminal vesicles and prostate) were removed, and the pathways used by sperm (the vas deferens) were cut.

Most doctors feel that regaining potency is helped along by attempting to get an erection as soon as possible once the body has had a chance to heal (usually about 6 weeks after the operation). Medicines (see below) may be helpful at this time. Be sure to talk to your doctor about your situation.

Several options may help you if you have erectile dysfunction:

*Phosphodiesterase inhibitors* such as sildenafil (Viagra), vardenafil (Levitra), and tadalafil (Cialis) are pills that can promote erections. These drugs will not work if both nerves have been damaged or removed. The most common side effects are headache, flushing (skin becomes red and feels warm), upset stomach, light sensitivity, and runny or stuffy nose. Nitrates, which are drugs used to treat heart disease, can interact with these drugs to cause very low blood pressure, which can be dangerous. Some other drugs may also cause problems, so be sure your doctor knows which medicines you are taking.

Some studies have found that these drugs may, in very rare cases, block blood flow to the optic nerve in the back of the eye. This could lead to blindness. Men who developed this complication often had a history of smoking or problems with high blood pressure, diabetes, or high levels of cholesterol or fat in their blood.

*Prostaglandin E1* is a substance naturally made in the body that can produce erections. A manmade version of this substance (alprostadil) can be injected almost painlessly into the base of the penis 5 to 10 minutes before intercourse or introduced into the tip of the penis as a suppository. You can even increase the dosage to prolong the erection. You may have side effects, such as pain, dizziness, and prolonged erection, but they are usually minimal.

*Vacuum devices* are another option that may create an erection. These mechanical pumps are placed around the entire penis before intercourse to produce an erection.

*Penile implants* might restore your ability to have erections if other methods do not help. An operation is needed to put them in place. There are several types of penile implants, including those using silicone rods or inflatable devices.

For more detailed information on coping with erection problems and other sexuality issues, see our document, *Sexuality and Cancer: For the Man Who Has Cancer and His Partner*.

**Sterility:** Radical prostatectomy cuts the connection between the testicles (where sperm are produced) and the urethra. This means that a man can no longer father a child by natural means. Often, this is not an issue, as men with prostate cancer tend to be older. But if it is a concern for you, you may want to speak with your doctor about "banking" your sperm before the operation.

**Lymphedema:** A rare but possible complication of removing many of the lymph nodes around the prostate (either surgically or laparoscopically) is a condition called lymphedema. Lymph nodes normally provide a way for fluid to return from all areas of the body to the heart. When nodes are removed, fluid may collect in the legs or genital region over time, causing swelling and pain. Lymphedema can usually be treated with physical therapy, although it may not disappear completely.

**Change in penis length:** A possible minor effect of surgery is a decrease in penis length. In one study, about 1 out of 5 men had a 15% or greater decrease in the length of their penis.

## Radiation Therapy

Radiation therapy uses high-energy rays or particles to kill cancer cells. Radiation is sometimes used as the initial treatment for low-grade cancer that is still confined within the prostate gland or that has only spread to nearby tissue. Cure rates for men with these types of cancers are much like those for men getting radical prostatectomy. Radiation is also sometimes used if the cancer is not completely removed or comes back (recurs) in the area of the prostate after surgery. If the disease is more advanced, radiation may be used to reduce the size of the tumor and to provide relief from present and possible future symptoms.

Two main types of radiation therapy are used: external beam radiation and brachytherapy (internal radiation). Both appear to be good methods of treating prostate cancer, although there is more long-term information about the results of treatment with external beam radiation.

### External Beam Radiation Therapy (EBRT)

In EBRT the radiation is focused on the prostate gland from a source outside your body. It is much like getting an x-ray but for a longer time. Before treatments start, imaging studies such as MRIs, CT scans, or plain x-rays of the pelvis are done to find the exact location of your prostate gland. The radiation team may then make some ink marks on your skin that



they will use later as a guide to focus the radiation in the right area. You will usually be treated 5 days per week in an outpatient center over a period of 7 to 9 weeks. Each treatment lasts only a few minutes and is painless.

Aside from being used as a treatment for early stage cancer, external beam radiation can also be used to help relieve bone pain when the cancer has spread to a specific area of bone.

Standard (conventional) EBRT is used much less often than in the past. Newer techniques allow doctors to be more accurate in treating the prostate gland while reducing the radiation exposure to nearby healthy tissues. These techniques appear to offer better chances of increasing the success rate and reducing side effects.

**Three-dimensional conformal radiation therapy (3D-CRT):** 3D-CRT uses special computers to precisely map the location of your prostate. You will likely be fitted with a plastic mold resembling a body cast to keep you in the same position so that the radiation can be aimed more accurately. Radiation beams are then shaped and aimed at the prostate from several directions, which makes it less likely to damage normal tissues.

Although the procedure is fairly new, the short-term results suggest that it is at least as effective as standard radiation therapy. Many doctors now recommend using it when it is available. In theory, by aiming the radiation more accurately, doctors can reduce radiation damage to tissues near the prostate and cure more cancers by increasing the radiation dose to the prostate. Long-term study results are still needed to confirm this.

**Intensity modulated radiation therapy (IMRT):** IMRT is an advanced form of 3D therapy. It uses a computer-driven machine that actually moves around the patient as it delivers radiation. In addition to shaping the beams and aiming them at the prostate from several angles, the intensity (strength) of the beams can be adjusted to minimize the dose reaching the most sensitive normal tissues. This allows doctors to deliver an even higher dose to the cancer areas. Many major hospitals and cancer centers are now able to provide IMRT.

**Conformal proton beam radiation therapy:** Proton beam therapy is related to 3D-CRT and uses a similar approach. But instead of using x-rays, this technique focuses proton beams on the cancer. Protons are positive parts of atoms. Unlike x-rays, which release energy both before and after they hit their target, protons cause little damage to tissues they pass through and then release their energy after traveling a certain distance. This means that proton beam radiation may be able to deliver more radiation to the prostate and do less damage to nearby normal tissues. As with 3D-CRT and IMRT, early results are promising, but more studies will be needed to show a long-term advantage over standard external beam radiation. The machines needed to make protons are expensive, and there are only a handful of them in use in the United States. Proton beam radiation may not be covered by all insurance companies at this time.

**Possible side effects of external beam radiation therapy:** The numbers used in describing the possible side effects below relate to standard external radiation therapy, which is now

used much less often than in the past. The risks of the newer treatment methods described above are likely to be lower.

**Bowel problems:** During and after treatment with external beam radiation therapy, you may have diarrhea, sometimes with blood in the stool, rectal leakage, and an irritated large intestine. Most of these problems go away over time, but in rare cases normal bowel function does not return after treatment ends. In the past, about 10% to 20% of men reported bowel problems after external beam radiation therapy, but the newer conformal radiation techniques may be less likely to cause these problems.

**Bladder problems:** You might have trouble with having to urinate often, a burning sensation while urinating, and blood in your urine. Bladder problems continue in about 1 out of 3 patients, with the most common problem being the need to urinate often.

**Urinary incontinence:** Although this side effect is less common than after surgery overall, the chance of incontinence goes up each year for several years after treatment.

**Impotence:** After several years, the impotence rate after radiation is about the same as that of surgery. It usually does not occur right after radiation therapy but slowly develops over a year or more. This is different from surgery, where impotence occurs immediately and may improve over time. In older studies, about 3 out of 4 men were impotent within 5 years of having external beam radiation therapy (some of these men had erection problems before treatment). In men who had normal erections before treatment, about half became impotent at 5 years. It's not clear if these numbers will apply to newer forms of radiation as well. As with surgery, the older you are, the more likely it is you will become impotent. Impotence may be helped by treatments such as those listed in the section above, including erectile dysfunction medicines.

**Feeling tired:** Radiation therapy may also cause fatigue that may not disappear until a few months after treatment stops.

**Lymphedema:** Fluid buildup in the legs or genitals (described in the surgery section of this document) is possible if the lymph nodes receive radiation.

### **Brachytherapy (Internal Radiation Therapy)**

Brachytherapy (also called *seed implantation* or *interstitial radiation therapy*) is the use of small radioactive pellets, or "seeds," each about the size of a grain of rice, that are placed directly into your prostate. Brachytherapy is generally used only in men with early stage prostate cancer that is relatively slow growing.

Its use may also be limited by other factors. For men who have had a transurethral resection of the prostate (TURP) or for those who already have urinary problems, the risk of urinary

side effects may be higher. Brachytherapy may not be as effective in men with large prostate glands because many more seeds may be needed. Doctors are now looking at ways of getting around this, such as giving men a short course of hormone therapy beforehand to shrink the prostate.

Imaging tests such as transrectal ultrasound, CT scans, or MRI help guide the placement of the radioactive pellets. Special computer programs calculate the exact dose of radiation needed. Without these, the cancer might get too little radiation or the normal tissues around it could get too much.

There are 2 types of prostate brachytherapy. Both are done in an operating room and require some type of anesthesia.

**Permanent (low dose rate, or LDR) brachytherapy:** In this approach, pellets (seeds) of radioactive material (such as iodine-125 or palladium-103) are placed inside thin needles, which are inserted through the skin in the area between the scrotum and anus (perineum) and into the prostate. The pellets are left in place as the needles are removed and give off low doses of radiation for weeks or months. Radiation from the seeds travels a very short distance, so the seeds can put out a very large amount of radiation to a very small area. This decreases the amount of damage done to the healthy tissues that are close to the prostate.

Usually, anywhere from 40 to 100 seeds are placed. Because they are so small, their presence causes little discomfort, and they are simply left in place after their radioactive material is used up. This type of radiation therapy requires spinal anesthesia (where the lower half of your body is numbed) or general anesthesia (where you are asleep) and may require 1 day in the hospital.

You may also receive external beam radiation along with brachytherapy, especially if there is a risk that your cancer has spread outside of the prostate (for example, if you have a high Gleason score).

**Temporary (high dose rate, or HDR) brachytherapy:** This is a newer technique. Hollow needles are placed through the perineum into the prostate. Soft nylon tubes (catheters) are placed in these needles. The needles are then removed but the catheters stay in place. Radioactive iridium-192 or cesium-137 is then placed in the catheters, usually for 5 to 15 minutes. Generally, about 3 brief treatments are given, and the radioactive substance is removed each time. The treatments are usually given over a couple of days. After the last treatment the catheters are removed. For about a week following placement of the catheters, you may have some pain in the area between your scrotum and rectum, and your urine may be reddish-brown.

These treatments are usually combined with external beam radiation given at a lower dose than if used by itself. The total dose of radiation is computed so that it is high enough to kill all the cancer cells. The advantage of this approach is that most of the radiation is

concentrated in the prostate gland itself, sparing the urethra and the tissues around the prostate such as the nerves, bladder, and rectum.

**Possible risks and side effects of brachytherapy:** If you receive permanent brachytherapy seeds, they will give off small amounts of radiation for several weeks. Even though the radiation doesn't travel far, your doctor may advise you to stay away from pregnant women and small children during this time. You may be asked to take other precautions as well, such as wearing a condom during sex.

There is also a small risk that some of the seeds may move (migrate). You may be asked to strain your urine for the first week or so to catch any seeds that might come out. Be sure to carefully follow any instructions your doctor gives you. There have also been reports of the seeds moving through the bloodstream to other parts of the body, such as the lungs. As far as doctors can tell, this doesn't seem to cause any ill effects and happens very rarely.

Like external beam radiation, brachytherapy can also cause impotence, urinary problems, and bowel problems.

**Bowel problems:** Significant long-term bowel problems (including burning and rectal pain and/or diarrhea) occur in less than 5% of patients.

**Urinary problems:** Severe urinary incontinence is not a common side effect. But frequent urination may persist in about 1 out of 3 patients who have brachytherapy. This is perhaps caused by irritation of the urethra, the tube that drains urine from the bladder. Rarely, this tube may actually close off (known as urethral stricture) and need to be opened with surgery.

**Impotence:** Problems with erections may be less likely to develop after brachytherapy than after other common forms of treatment, but this is unclear. Some studies have found rates of sexual dysfunction to be lower after brachytherapy, but other studies have found that the impotence rates were no lower than with external beam radiation or surgery. Again, the younger you are and the better your sexual function before treatment, the more likely you will be to regain function after treatment.

## Cryosurgery

Cryosurgery (also called cryotherapy or cryoablation) is sometimes used to treat localized prostate cancer by freezing it. As with brachytherapy, this may not be a good option for men with large prostate glands.

In this approach, several hollow probes (needles) are placed through the skin between the anus and scrotum (the perineum). The doctor guides them into the prostate using transrectal ultrasound (TRUS). Very cold gases are passed through the needles, creating ice balls that destroy the prostate gland. To be sure prostate tissue is destroyed without too much damage to nearby tissues, the doctor carefully watches the ultrasound images during the procedure.

Warm saltwater is circulated through a catheter in the urethra to keep it from freezing. Spinal, epidural, or general anesthesia is used during the procedure.

Before cryosurgery a suprapubic catheter is placed through a skin incision on the abdomen and into the bladder so that if the prostate swells after the procedure (which usually occurs), urine can be drained through this tube. The catheter is removed a couple of weeks later, once the swelling goes down. After the procedure, there will be some bruising and soreness in the perineum where the probes were inserted. You will likely stay in the hospital for a day.

Cryosurgery is less invasive than radical prostatectomy, so there is usually less blood loss, a shorter hospital stay, shorter recovery period, and less pain than with surgery. But compared with surgery or radiation therapy, doctors know much less about the long-term effectiveness of cryosurgery. Current techniques using ultrasound guidance and precise temperature monitoring have only been available for a few years. Outcomes of long-term (10- to 15-year) follow-up must still be collected and reviewed. For this reason, most doctors do not include cryotherapy among the options they routinely consider for the first treatment of prostate cancer. It is sometimes recommended if the cancer has come back after other treatments.

### **Possible Side Effects of Cryosurgery**

Side effects from cryosurgery tend to be worse if it is done in men who have already had radiation therapy, as opposed to men who have it as the first form of treatment.

Most men have blood in their urine for a day or two after the procedure, as well as soreness in the area where the needles were placed. Swelling of the penis or scrotum is also common. The freezing may also affect the bladder and intestines, which can lead to pain, burning sensations, and the need to empty the bladder and bowels often. Most men recover normal bowel and bladder function over time.

Freezing damages nerves near the prostate and causes impotence in up to 80% of men who have cryosurgery. Erectile dysfunction is more common after cryosurgery than after radical prostatectomy (see above).

Urinary incontinence is rare in men who have cryosurgery as their first treatment for prostate cancer, but it is more common in men who have already had radiation therapy.

A fistula (an abnormal connection) between the rectum and bladder develops in less than 1% of men after cryosurgery. This rare but serious problem can allow urine to leak into the rectum and may require surgery to repair.

### **Hormone (Androgen Deprivation) Therapy**

Hormone therapy is also called androgen deprivation therapy (ADT) or androgen suppression therapy. The goal is to reduce levels of the male hormones, called androgens, in the body. The main androgens are testosterone and dihydrotestosterone (DHT). Androgens, produced mainly in the testicles, stimulate prostate cancer cells to grow. Lowering androgen levels

often makes prostate cancers shrink or grow more slowly. However, hormone therapy does not cure prostate cancer.

Hormone therapy may be used in several situations:

- if you are not able to have surgery or radiation or can't be cured by these treatments because the cancer has already spread beyond the prostate gland
- if your cancer remains or comes back after treatment with surgery or radiation therapy
- as an addition to radiation therapy as initial treatment if you are at high risk for cancer recurrence
- before surgery or radiation to try and shrink the cancer to make other treatments more effective

### **Types of Hormone Therapy**

There are several types of hormone therapy used to treat prostate cancer.

**Orchiectomy (surgical castration):** Even though this is a type of surgery, its main effect is as a form of hormone therapy. In this operation, the surgeon removes the testicles, where more than 90% of the androgens, mostly testosterone, are made. With this source removed, most prostate cancers stop growing or shrink for a time.

This is done as a simple outpatient procedure. It is probably the least expensive and simplest way to reduce androgen levels in the body. But unlike some of the other methods of lowering androgen levels, it is permanent, and many men have trouble accepting the removal of their testicles. Some men having the procedure are concerned about how it will look. If wanted, artificial silicone sacs filled with saline (salt water) can be inserted into the scrotum. These look and feel like testicles.

Possible *side effects* of orchiectomy are generally related to changing levels of hormones in the body. About 90% of men who have had this operation have reduced or absent libido (sexual desire) and impotence. Some men also experience:

- hot flashes (these may go away with time)
- breast tenderness and growth of breast tissue
- osteoporosis (bone thinning) which can lead to broken bones
- anemia (low red blood cell counts)
- decreased mental acuity (sharpness)
- loss of muscle mass
- weight gain
- fatigue
- decrease in HDL ("good") cholesterol
- depression

Many of these side effects can be prevented or treated. For example, sometimes the hot flashes will be helped by treatment with antidepressants. Brief radiation treatment to the breasts before surgery can help prevent their enlargement.

Men getting this treatment should be watched and treated for osteoporosis to help prevent broken bones. There are several different drugs available. Exercise is a good way to reduce fatigue, weight gain, and the chance of loss of bone and muscle mass. If anemia occurs, it is often very mild and usually doesn't cause symptoms. Depression can be treated by antidepressants and/or counseling.

**Luteinizing hormone-releasing hormone (LHRH) analogs:** Even though LHRH analogs (also called LHRH agonists) cost more and require more frequent doctor visits, most men choose this method over orchiectomy. These drugs lower testosterone levels just as well as orchiectomy by lowering the levels of androgens (mainly testosterone) made by your testicles.

LHRH analogs are injected or placed as small implants under the skin. They are given either monthly or every 3, 4, 6, or 12 months. The LHRH analogs available in the United States include leuprolide (Lupron, Viadur, Eligard), goserelin (Zoladex), and triptorelin (Trelstar).

Possible *side effects* of LHRH analogs such as hot flashes, osteoporosis, and others are similar to those of orchiectomy (see above), and are largely due to low testosterone levels.

When LHRH analogs are first given, testosterone production increases briefly before falling to very low levels. This effect is called *flare* and results from the complex way in which LHRH analogs work. Men whose cancer has spread to the bones may experience bone pain. If the cancer has spread to the spine, even a short-term increase in growth could compress the spinal cord and cause pain or paralysis. Flare can be avoided by giving drugs called anti-androgens for a few weeks when starting treatment with LHRH analogs. (For more on anti-androgens, see below.)

**Luteinizing hormone-releasing hormone (LHRH) antagonists:** A newer drug, abarelix (Plenaxis), is an LHRH antagonist. It is thought to work like LHRH agonists, but it appears to reduce testosterone levels more quickly and does not cause tumor flare like the LHRH agonists do.

A small percentage of men (fewer than 5%) have serious allergic reactions to the drug. Because of this, it is only approved for use in men who have serious symptoms from advanced prostate cancer and who cannot or refuse to take other forms of hormone therapy.

The possible side effects are similar to those with orchiectomy (see above) or LHRH agonists.

Abarelix is given only in qualified doctors' offices. It is injected into the buttocks every 2 weeks for the first month, then every 4 weeks. You will be asked to remain in the office for 30 minutes after the injection to make sure you are not having an allergic reaction.

**Anti-androgens:** Anti-androgens block the body's ability to use any androgens. Even after orchiectomy or during treatment with LHRH analogs, a small amount of androgens is still made by the adrenal glands.

Drugs of this type, such as flutamide (Eulexin), bicalutamide (Casodex), and nilutamide (Nilandron), are taken daily as pills.

Anti-androgens are not often used by themselves (see below). An anti-androgen may be added if treatment with orchiectomy or an LHRH analog is no longer working by itself.

Anti-androgen treatment may be combined with orchiectomy or LHRH analogs as first-line hormone therapy. This is called combined androgen blockade (CAB). There is still some debate as to whether CAB is more effective in this setting than using orchiectomy or an LHRH analog alone. If there is a benefit, it appears to be small.

Some doctors are testing the use of anti-androgens *instead of* orchiectomy or LHRH analogs. Several recent studies have compared the effectiveness of anti-androgens alone with that of LHRH agonists. Most found no difference in survival rates, but a few found anti-androgens to be slightly less effective.

If hormone therapy including an anti-androgen stops working, some men seem to benefit for a short time from simply stopping the anti-androgen. Doctors call this the "anti-androgen withdrawal" effect, although they are not sure why it happens.

*Side effects* of anti-androgens in patients already being treated by orchiectomy or with LHRH agonists are usually not serious. Diarrhea is the major side effect, although nausea, liver problems, and tiredness can also occur.

The major difference from LHRH agonists and orchiectomy is that anti-androgens may have fewer sexual side effects. When these drugs are used alone libido and potency can often be maintained.

**Other androgen-suppressing drugs:** Estrogens were once the main alternative to orchiectomy for men with advanced prostate cancer. Because of their possible side effects (including blood clots and breast enlargement), estrogens have been largely replaced by LHRH analogs and anti-androgens. Still, estrogens may be tried if androgen deprivation is no longer working.

Ketoconazole (Nizoral), first used for treating fungal infections, blocks production of androgens and is sometimes used.



## **Current Controversies in Hormone Therapy**

There are many issues around hormone therapy that not all doctors agree on, such as the best time to start and stop it and the best way to give it. Studies looking at these issues are now under way. A few of the issues are discussed here.

**Early vs. delayed treatment:** Some doctors think that hormone therapy works better if it is started as soon as possible if the cancer has reached an advanced stage (for example, when it has spread to lymph nodes), if it is large (T3) or has a high Gleason score, or if the PSA starts rising after initial therapy, even though the patient feels well. Some studies have shown that hormone treatment may slow down the disease and perhaps even lengthen patient survival. But not all doctors agree with this approach. Some are waiting for more evidence of benefit. They feel that because of the likely side effects and the chance that the cancer could become resistant to therapy sooner, treatment should not be started until symptoms from the disease appear. Studies addressing these questions are now under way.

**Intermittent vs. continuous hormone therapy:** Nearly all prostate cancers treated with hormone therapy become resistant to this treatment over a period of months or years. Some doctors believe that constant androgen suppression may not be needed, so they advise intermittent (on-again, off-again) treatment.

In one form of intermittent therapy, androgen suppression is stopped once the blood PSA level drops to a very low level. If the PSA level begins to rise, the drugs are started again. Another form of intermittent therapy involves using androgen suppression for fixed periods of time -- for example, 6 months on followed by 6 months off.

Clinical trials of intermittent hormonal therapy are still in progress. It is too early to say whether this new approach is better or worse than continuous hormonal therapy. However, one advantage of intermittent treatment is that for a while some men are able to avoid the side effects of hormonal therapy such as impotence, hot flashes, and loss of sex drive.

**Combined androgen blockade (CAB):** Some doctors treat patients with both androgen deprivation (orchiectomy or an LHRH agonist) and an anti-androgen. But most doctors are not convinced there's enough evidence that this combined therapy is better than one drug alone.

**Triple androgen blockade (TAB):** Some doctors have suggested taking combined therapy one step further, by adding a drug called a 5-alpha reductase inhibitor -- either finasteride (Proscar, Propecia) or dutasteride (Avodart) -- to the combined androgen blockade. There is very little evidence to support the use of this "triple androgen blockade" at this time.

## **Chemotherapy**

Chemotherapy is sometimes used if prostate cancer has spread outside of the prostate gland and hormone therapy isn't working. It is not recommended as a treatment if you have early prostate cancer.

Chemotherapy uses anti-cancer drugs injected into a vein or given by mouth. These drugs enter the bloodstream and go throughout the body, making this treatment potentially useful for cancers that have spread (metastasized) to distant organs.

At one time, chemotherapy was not thought to be very effective in treating prostate cancer, but this has changed in recent years. A combination of the chemotherapy drug docetaxel (Taxotere) and the steroid drug prednisone has been shown to reduce symptoms and prolong life (when compared with other chemotherapy drugs) in patients with advanced prostate cancer. Most doctors now consider this to be the first-line chemotherapy option in men whose cancer is no longer responding to hormonal treatments.

Some of the other chemotherapy drugs used to treat prostate cancer include:

- mitoxantrone (Novantrone)
- estramustine (Emcyt)
- doxorubicin (Adriamycin)
- etoposide (VP-16)
- vinblastine (Velban)
- paclitaxel (Taxol)
- carboplatin (Paraplatin)
- vinorelbine (Navelbine)

Like hormone therapy, chemotherapy is unlikely to result in a cure. This treatment is not expected to destroy all the cancer cells, but it may slow the cancer's growth and reduce symptoms, resulting in a better quality of life.

### **Possible Side Effects of Chemotherapy**

Chemotherapy drugs work by attacking cells that are dividing quickly, which is why they work against cancer cells. But other cells in the body, such as those in the bone marrow, the lining of the mouth and intestines, and the hair follicles, also divide quickly. These cells are also likely to be affected by chemotherapy, which can lead to side effects.

The side effects of chemotherapy depend on the type and dose of drugs given and the length of time they are taken. These side effects may include:

- hair loss
- mouth sores
- loss of appetite
- nausea and vomiting
- lowered resistance to infection (due to low white blood cell counts)
- easy bruising or bleeding (due to low blood platelets)
- fatigue (due to low red blood cells)

In addition, each chemotherapy drug may have its own unique side effects. For example, estramustine, a drug sometimes used to treat prostate cancer, also carries the risk of blood clots.

The side effects of chemotherapy are usually short-term and go away once treatment is finished. There is help for many of these side effects. For example, drugs can be given to prevent or reduce nausea and vomiting. Other drugs can be given to boost blood cell counts.

## **Treatment of Pain**

Most of this document discusses ways to remove or to destroy prostate cancer cells or to slow their growth. But maintaining your quality of life is another important goal. Don't hesitate to discuss pain, other symptoms, or any quality of life concerns with your cancer care team. Pain and most other symptoms of prostate cancer can often be treated effectively. If the treatments listed above don't help with symptoms, there are several other options.

### **Pain Medicines**

When properly prescribed, pain medicines (ranging from aspirin to opioids) are very effective. Although you may worry about addiction or dependence with opioids, this is almost never a problem if you have cancer pain. Symptoms such as drowsiness and constipation are possible but can usually be treated by changing the dose or by adding other medicines.

### **Bisphosphonates**

Bisphosphonates are a group of drugs that can help relieve bone pain caused by cancer that has spread (metastasized). These drugs may also slow the growth of the metastases and prevent fractures. Bisphosphonates may have the added benefit of strengthening bones in men who are also receiving hormone therapy. The most commonly used bisphosphonate is zoledronic acid (Zometa), which is approved for use in bone metastases from prostate cancer. It is given as an intravenous (IV) injection. Other bisphosphonates have been approved for other uses, and some doctors use these "off label" (to treat a condition for which they have not been approved by the Food and Drug Administration) to treat prostate cancer.

Bisphosphonates can have their own side effects, including flu-like symptoms and bone pain. A rare but very distressing side effect of bisphosphonates is damage (osteonecrosis) in the jaw bones. This can lead to loss of teeth or infections of the jaw bone. Doctors don't know why this happens or how to prevent it, other than to stop the bisphosphonates. Maintaining good oral hygiene by flossing, brushing, making sure that dentures fit properly, and having regular dental checkups may help prevent this. Some cancer doctors recommend that patients have a dental checkup and have any tooth or jaw problems treated before they start taking bisphosphonates.

### **Steroids**

Some studies suggest that corticosteroids (such as prednisone and dexamethasone) can help relieve bone pain in some men.

### **External Radiation Therapy**

Radiation therapy can help reduce bone pain, especially if the pain is limited to one or only a few areas of bone. Radiation can be aimed at tumors on the spine, which can help relieve

pressure on the spinal cord in some cases. Radiation therapy may also help relieve other symptoms by shrinking tumors in other parts of the body.

**Radiopharmaceuticals:** Strontium-89 (Metastron) and Samarium-153 (Quadramet) are drugs that contain radioactive elements. They are injected into a vein and collect in bones. Once there, the radiation they give off kills the cancer cells and relieves some of the pain caused by bone metastases. About 80% of prostate cancer patients with painful bone metastases are helped by this treatment.

These drugs are used to treat bone pain caused by metastatic prostate cancer, not early stage prostate cancer. If prostate cancer has spread to many bones, this approach is much better than trying to aim external beam radiation at each affected bone. In some cases, these drugs are used together with external beam radiation aimed at the most painful bone metastases.

The major side effect of this treatment is a lowering of blood cell counts, which could place you at increased risk for infections or bleeding, especially if your counts are already low.

It is very important that your pain be treated effectively. This will help you feel better and allow you to focus on the people and activities that are most important to you.

## **Clinical Trials**

You have had to make a lot of decisions since you've been told you have cancer. One of the most important decisions you will make is deciding which treatment is best for you. You may have heard about clinical trials being done for your type of cancer. Or maybe someone on your health care team has mentioned a clinical trial to you. Clinical trials are one way to get state-of-the-art cancer care. Still, they are not right for everyone.

Here we will give you a brief review of clinical trials. Talking to your health care team, your family, and your friends can help you make the best treatment choice for you.

### **What Are Clinical Trials?**

Clinical trials are carefully controlled research studies that are done with patients. These studies test whether a new treatment is safe and how well it works in patients, or they may test new ways to diagnose or prevent a disease. Clinical trials have led to many advances in cancer prevention, diagnosis, and treatment.

### **The Purpose of Clinical Trials**

Clinical trials are done to get a closer look at promising new treatments or procedures in patients. A clinical trial is only done when there is good reason to believe that the treatment, test, or procedure being studied may be better than the one used now. Treatments used in clinical trials are often found to have real benefits and may go on to become tomorrow's standard treatment.

Clinical trials can focus on many things, such as:

- new uses of drugs that are already approved by the US Food and Drug Administration (FDA)
- new drugs that have not yet been approved by the FDA
- non-drug treatments (such as radiation therapy)
- medical procedures (such as types of surgery)
- herbs and vitamins
- tools to improve the ways medicines or diagnostic tests are used
- medicines or procedures to relieve symptoms or improve comfort
- combinations of treatments and procedures

Researchers conduct studies of new treatments to try to answer the following questions:

- Is the treatment helpful?
- What's the best way to give it?
- Does it work better than other treatments already available?
- What side effects does the treatment cause?
- Are there more or fewer side effects than the standard treatment used now?
- Do the benefits outweigh the side effects?
- In which patients is the treatment most likely to be helpful?

### **Phases of Clinical Trials**

There are 4 phases of clinical trials, which are numbered I, II, III, and IV. We will use the example of testing a new cancer treatment drug to look at what each phase is like.

**Phase I clinical trials:** The purpose of a phase I study is to find the best way to give a new treatment safely to patients. The cancer care team closely watches patients for any harmful side effects.

For phase I studies, the drug has already been tested in lab and animal studies, but the side effects in patients are not fully known. Doctors start by giving very low doses of the drug to the first patients and increase the doses for later groups of patients until side effects appear or the desired effect is seen. Doctors are hoping to help patients, but the main purpose of a phase I trial is to test the safety of the drug.

Phase I clinical trials are often done in small groups of people with different cancers that have not responded to standard treatment, or that keep coming back (recurring) after treatment. If a drug is found to be reasonably safe in phase I studies, it can be tested in a phase II clinical trial.

**Phase II clinical trials:** These studies are designed to see if the drug works. Patients are given the best dose as determined from phase I studies. They are closely watched for an effect on the cancer. The cancer care team also looks for side effects.

Phase II trials are often done in larger groups of patients with a specific cancer type that has not responded to standard treatment. If a drug is found to be effective in phase II studies, it can be tested in a phase III clinical trial.

**Phase III clinical trials:** Phase III studies involve large numbers of patients -- most often those who have just been diagnosed with a specific type of cancer. Phase III clinical trials may enroll thousands of patients.

Often, these studies are randomized. This means that patients are randomly put in one of two (or more) groups. One group (called the control group) gets the standard, most accepted treatment. Another group (or more than one group) will get the new treatment being studied. All patients in phase III studies are closely watched. The study will be stopped early if the side effects of the new treatment are too severe or if one group has much better results than the others.

Phase III clinical trials are usually needed before the FDA will approve a treatment for use by the general public.

**Phase IV clinical trials:** Once a drug has been approved by the FDA and is available for all patients, it is still studied in other clinical trials (sometimes referred to as phase IV studies). This way more can be learned about short-term and long-term side effects and safety as the drug is used in larger numbers of patients with many types of diseases. Doctors can also learn more about how well the drug works, and if it might be helpful when used in other ways (such as in combination with other treatments).

### **What It Will Be Like to Be in a Clinical Trial**

If you are in a clinical trial, you will have a team of experts taking care of you and watching your progress very carefully. Depending on the phase of the clinical trial, you may receive more attention (such as having more doctor visits and lab tests) than you would if you were treated outside of a clinical trial. Clinical trials are specially designed to pay close attention to you.

However, there are some risks. No one involved in the study knows in advance whether the treatment will work or exactly what side effects will occur. That is what the study is designed to find out. While most side effects go away in time, some may be long-lasting or even life threatening. Keep in mind, though, that even standard treatments have side effects. Depending on many factors, you may decide to enter (enroll in) a clinical trial.

### **Deciding to Enter a Clinical Trial**

If you would like to take part in a clinical trial, you should begin by asking your doctor if your clinic or hospital conducts clinical trials. There are requirements you must meet to take part in any clinical trial. But whether or not you enter (enroll in) a clinical trial is completely up to you.

Your doctors and nurses will explain the study to you in detail. They will go over the possible risks and benefits and give you a form to read and sign. The form says that you understand the clinical trial and want to take part in it. This process is known as giving your informed consent. Even after reading and signing the form and after the clinical trial begins, you are free to leave the study at any time, for any reason. Taking part in a clinical trial does not keep you from getting any other medical care you may need.

To find out more about clinical trials, talk to your cancer care team. Here are some questions you might ask:

- Is there a clinical trial that I could take part in?
- What is the purpose of the study?
- What kinds of tests and treatments does the study involve?
- What does this treatment do? Has it been used before?
- Will I know which treatment I receive?
- What is likely to happen in my case with, or without, this new treatment?
- What are my other choices and their pros and cons?
- How could the study affect my daily life?
- What side effects can I expect from the study? Can the side effects be controlled?
- Will I have to stay in the hospital? If so, how often and for how long?
- Will the study cost me anything? Will any of the treatment be free?
- If I am harmed as a result of the research, what treatment would I be entitled to?
- What type of long-term follow-up care is part of the study?
- Has the treatment been used to treat other types of cancers?

### **How Can I Find Out More About Clinical Trials That Might Be Right for Me?**

The American Cancer Society offers a clinical trials matching service for patients, their family, and friends. You can reach this service at 1-800-303-5691 or on our Web site at <http://clinicaltrials.cancer.org>.

Based on the information you give about your cancer type, stage, and previous treatments, this service can put together a list of clinical trials that match your medical needs. The service will also ask where you live and whether you are willing to travel so that it can look for a treatment center that you can get to.

You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials Web site at [www.cancer.gov/clinicaltrials](http://www.cancer.gov/clinicaltrials).

For even more information on clinical trials, the American Cancer Society has a document called *Clinical Trials: What You Need to Know*. You can read this on the Web site, [www.cancer.org](http://www.cancer.org), or have it sent to you by calling 1-800-ACS-2345.

## **Complementary and Alternative Therapies**

When you have cancer you are likely to hear about ways to treat your cancer or relieve symptoms that are different from mainstream (standard) medical treatment. These methods can include vitamins, herbs, and special diets, or methods such as acupuncture or massage—among many others. You may have a lot of questions about these treatments. Here are some you may have thought of already:

- How do I know if a non-standard treatment is safe?
- How do I know if it works?
- Should I try one or more of these treatments?
- What does my doctor know/think about these methods? Should I tell the doctor that I'm thinking about trying them?
- Will these treatments cause a problem with my standard medical treatment?
- What is the difference between "complementary" and "alternative" methods?
- Where can I find out more about these treatments?

### **The Terms Can Be Confusing**

Not everyone uses these terms the same way, so it can be confusing. The American Cancer Society uses *complementary* to refer to medicines or methods that are used *along with* your regular medical care. *Alternative* medicine is a treatment used *instead of* standard medical treatment.

**Complementary Methods:** Complementary treatment methods, for the most part, are not presented as cures for cancer. Most often they are used to help you feel better. Some methods that can be used in a complementary way are meditation to reduce stress, acupuncture to relieve pain or peppermint tea to relieve nausea. There are many others. Some of these methods are known to help, while others have not been tested. Some have been proven not be helpful. A few have even been found harmful. However, some of these methods may add to your comfort and well-being.

There are many complementary methods that you can safely use right along with your medical treatment to help relieve symptoms or side effects, to ease pain, and to help you enjoy life more. For example, some people find methods such as aromatherapy, massage therapy, meditation, or yoga to be useful.

**Alternative Treatments:** Alternative treatments are those that are used instead of standard medical care. These treatments have not been proven safe and effective in clinical trials. Some of these methods may even be dangerous and some have life-threatening side effects. The biggest danger in most cases is that you may lose the chance to benefit from standard treatment. Delays or interruptions in your standard medical treatment may give the cancer more time to grow.

### **Deciding What to Do**

It is easy to see why people with cancer may consider alternative methods. You want to do all you can to fight the cancer. Sometimes mainstream treatments such as chemotherapy can be hard to take, or they may no longer be working.



Sometimes people suggest that their method can cure your cancer without having serious side effects, and it's normal to want to believe them. But the truth is that most non-standard methods of treatment have not been tested and proven to be effective for treating cancer.

As you consider your options, here are 3 important steps you can take:

- Talk to your doctor or nurse about any method you are thinking about using.
- Check the list of "red flags" below.
- Contact the American Cancer Society at 1-800-ACS-2345 to learn more about complementary and alternative methods in general and to learn more about the specific methods you are thinking about.

### **Red Flags**

You can use the questions below to spot treatments or methods to avoid. A "yes" answer to any one of these questions should raise a "red flag."

- Does the treatment promise a cure for all or most cancers?
- Are you told not to use standard medical treatment?
- Is the treatment or drug a "secret" that only certain people can give?
- Does the treatment require you to travel to another country?
- Do the promoters attack the medical or scientific community?

### **The Decision Is Yours**

Decisions about how to treat or manage your cancer are always yours to make. If you are thinking about using a complementary or alternative method, be sure to learn about the method and talk to your doctor about it. With reliable information and the support of your health care team, you may be able to safely use the methods that can help you while avoiding those that could be harmful.

### **Considering Prostate Cancer Treatment Options**

If you have prostate cancer, there are many important factors to take into account before deciding on a treatment option, such as your age and general health, and the likelihood that the cancer will cause problems for you. You should also think about which side effects you can live with. Some men, for example, can't imagine living with side effects such as incontinence or impotence. Other men are less concerned about these and more concerned about removing or destroying the cancer.

If you are older or have other serious health problems and your cancer is slow growing, you might find it helpful to think of prostate cancer as a chronic disease that will probably not lead to your death but may cause symptoms you want to avoid. You may be more inclined to consider watchful waiting (careful follow-up with your doctor) or hormone therapy, and less inclined to consider treatments that are likely to cause major side effects, such as radiation and surgery. Of course, age itself is not necessarily the best basis on which to make your

choice. Many men are in good mental and physical shape at age 70, while some younger men may not be as healthy.

If you are younger and otherwise healthy, you might be more willing to put up with the side effects of treatment if they offer you the best chance for cure. Most doctors now believe that external radiation, radical prostatectomy, and brachytherapy (radioactive implants) have about the same cure rates for the earliest stage prostate cancers. However, there are pros and cons to each type of treatment that should be considered, including possible risks and side effects (described above).

This is complicated even further by the explosion of newer types of surgery (laparoscopic prostatectomy and robotic-assisted prostatectomy) and radiation therapy (conformal radiation therapy, intensity-modulated radiation therapy, proton beam radiation, etc.) in recent years. Many of these appear very promising, but there is very little long-term data on them, which means comparing them to each other is very difficult, if not impossible.

Such a complex decision is often hard to make by yourself. You may find it helpful to talk with your family and friends before making a decision. It's important to note that prostate cancer is not a uniform disease, and each man's experience with it is different. Just because someone you know had a good (or bad) experience with a certain type of treatment doesn't necessarily mean the same will be true for you.

You may also want to consider getting more than one medical opinion, perhaps even from different types of doctors. For early stage cancers, it is natural for surgical specialists, such as urologists, to favor surgery and for radiation oncologists to lean more toward radiation. Doctors specializing in newer types of treatment may be more likely to recommend their therapies. Talking to each of them may give you a better perspective on your options. Your primary care doctor may also be helpful in sorting out which treatment might be right for you.

You might find that speaking with others who have faced or are currently facing the same issues is useful. The American Cancer Society's program, Man to Man, and similar programs sponsored by other organizations provide a forum for you to meet and discuss these and other cancer-related issues. For more information about our programs, call us toll-free at 1-800-ACS-2345 or visit our Web site at [www.cancer.org](http://www.cancer.org).

The information in the following sections describes the main treatment options available for prostate cancer in different situations. Before deciding on treatment, here are some further questions you may want to ask yourself:

- Are you the type of person who needs to do something about your cancer, even if it might result in serious side effects? Or would you be comfortable with watchful waiting, even if it means you might have more anxiety (and need more frequent follow-up) in the future?

- Do you feel the need to know right away whether your doctor thinks he or she was able to get all of the cancer out (a reason some men choose surgery)? Or are you comfortable with not knowing the results of treatment for a while (as is the case in radiation therapy) if it means not having to have surgery?
- Do you prefer to go with the newest technology, which may have some theoretical advantages? Or do you prefer to go with treatment methods that are better proven and with which doctors may have more experience?
- Which potential treatment side effects (incontinence, impotence, bowel problems) might be most distressing to you?
- How important for you are issues like the amount of time spent in treatment or recovery?
- If your initial treatment is not successful, what would your options be at that point?

Many men find it very stressful to have to choose between treatment options, and are very fearful they will choose the "wrong" one. In many cases, there is no single best option. It's important to take your time and decide which option is right for you.

## **Initial Treatment of Prostate Cancer by Stage**

The "How Is Prostate Cancer Staged?" section of this document explains how the T, N, and M classifications are used to stage your cancer. The stage of your cancer is one of the most important factors in choosing the best way to treat it.

What follows is a description of the treatments that may be options for men with prostate cancer diagnosed at a specific stage. But keep in mind that other factors, such as age, life expectancy, and risk of cancer recurrence after treatment (based on factors like Gleason score and PSA level) must also be taken into account when looking at treatment options.

### **Stage I**

These prostate cancers are small and have low Gleason scores. They usually grow very slowly and may never cause any symptoms or other health problems.

For men without any prostate cancer symptoms who are elderly and/or have other serious health problems, watchful waiting or radiation therapy (external beam or brachytherapy) are reasonable options.

Men who are younger and healthy may consider watchful waiting, radical prostatectomy, or radiation therapy (external beam or brachytherapy).

### **Stage II**

Compared with stage I prostate cancers, stage II cancers that are not treated with surgery or radiation are more likely to eventually spread beyond the prostate and cause symptoms.

As with stage I cancers, watchful waiting by following PSA levels is often a good option for men whose cancer is not causing any symptoms and who are elderly and/or have other serious health problems. Radical prostatectomy and radiation therapy (external beam or brachytherapy) may also be appropriate options.

Treatment options for men who are younger and otherwise healthy may include:

- radical prostatectomy (often with removal of the pelvic lymph nodes). This may be followed by external beam radiation if your cancer is found to have spread beyond the prostate at the time of surgery, or if the PSA level is still detectable several weeks after surgery.
- external beam radiation only\*
- brachytherapy only\*
- brachytherapy and external beam radiation combined\*
- taking part in a clinical trial of newer treatments

\* All the radiation options may be combined with several months of hormone therapy if there is a greater chance of recurrence based on PSA level and/or Gleason score.

### **Stage III**

Stage III cancers have spread beyond the prostate gland but have not reached the bladder, rectum, lymph nodes, or distant organs. Treatments such as surgery and radiation therapy may be less likely to cure, but may still be options.

Treatment options at this stage may include:

- external beam radiation plus hormone therapy
- hormone therapy only
- radical prostatectomy in selected cases (often with removal of the pelvic lymph nodes). This may be followed by radiation therapy.
- watchful waiting for older men whose cancer is causing no symptoms or for those who have another more serious illness
- taking part in a clinical trial of newer treatments

### **Stage IV**

Stage IV cancers have already spread to the bladder, rectum, lymph nodes, or distant organs such as the bones. These cancers are generally not considered to be curable.

Treatment options may include:

- hormone therapy
- external beam radiation plus hormone therapy (in selected cases)
- surgery (TURP) to relieve symptoms such as bleeding or urinary obstruction

- watchful waiting for older men whose cancer is causing no symptoms or for those who have another serious illness
- taking part in a clinical trial of newer treatments

If symptoms are not relieved by standard treatments and the cancer continues to grow and spread, chemotherapy may be an option. You may also want to think about taking part in a clinical trial. Treatment of stage IV prostate cancer may also include treatments for relief of symptoms such as bone pain.

## **Following PSA Levels After Treatment Meant to Cure Prostate Cancer**

The PSA level is often a good indicator of whether or not initial treatment was successful. Generally speaking, your PSA level should get very low after treatment. But PSA results aren't always cut and dry, and sometimes doctors aren't sure what they mean.

### **After Surgery**

The PSA should fall to an undetectable level within a couple of months after radical prostatectomy. Because some PSA may remain in the blood for several weeks after surgery, even if all of the prostate cells were removed, doctors often advise waiting at least 6 to 8 weeks after surgery before getting the test.

In recent years, blood tests have become much more sensitive -- so sensitive that they can detect very small amounts of PSA. While this would seem to be a good thing, it has made it more difficult to define exactly what an "undetectable" PSA level is. For example, a PSA of 0.5 ng/mL after surgery might be concerning, but doctors aren't sure whether this is also true of levels of 0.01 or 0.02 ng/mL. Some doctors would advise following such PSA levels over time to get a better idea of what may be going on, possibly with repeat tests every few months. Others might be more inclined to recommend further treatment. Of course, this uncertainty can be very stressful for patients and their families.

### **After Radiation Therapy**

The different types of radiation therapy don't kill all of the cells in the prostate gland, so they're not expected to cause the PSA to drop to an undetectable level. The remaining normal prostate cells will continue to make some PSA.

The pattern of the drop in PSA is also different than with surgery. PSA levels after radiation tend to drop gradually, and may not reach their lowest level until 2 years or more after treatment.

Doctors tend to follow the PSA levels every few months to look for trends. A one-time, small rise in PSA might be a cause for closer monitoring, but it may not necessarily mean that the cancer has returned, as PSA levels may fluctuate slightly from time to time. However, a PSA that is rising on consecutive tests after treatment might indicate that cancer is still present. Some medical groups have proposed that a PSA rise of more than 2 ng/mL above the lowest level it reached should be used as the cutoff point, but it's not clear if all doctors agree with this.

There is also a phenomenon called a "PSA bounce" that sometimes happens after radiation therapy. The PSA rises slightly for a short time within the first couple of years after treatment, but then falls back down. Doctors aren't sure why this happens, but it doesn't seem to have an effect on a patient's prognosis.

## **Prostate Cancer That Remains or Recurs After Treatment**

If the PSA level shows that the prostate cancer has not been cured or has come back (recurred) after an initial attempt to cure it, follow-up therapy will depend on where the cancer is thought to be located and what treatment(s) you have already had. (Usually, the same type of treatment is not an option because of the increased potential for serious side effects. For example, men who have already had radiation therapy cannot have radiation therapy again.) Imaging tests such as CT, MRI, or bone scans may be done to get a better idea about where the cancer may be.

If the cancer is still thought to be localized to the area of the prostate, a second attempt at curative treatment may be possible. If you've had a radical prostatectomy, radiation therapy may be an option. If your first treatment was radiation, radical prostatectomy may still be an option in selected cases, although it carries a high risk for potential side effects. Cryosurgery may also be an option if the cancer is still localized.

If the cancer has spread outside the prostate gland, it will most likely go first to nearby lymph nodes, and then to the bones. Much less often the cancer will spread to the liver or other organs.

If it has spread to other parts of the body (including the bones), hormone therapy is probably the most effective treatment, although it is very unlikely to cure the cancer. Usually the first treatment is an LHRH analog. If this stops working, an anti-androgen may be added. Other hormonal agents such as ketoconazole or estrogens (female hormones) may be helpful and can sometimes slow or stop the cancer from growing. Hormone therapy will be given as long as the cancer is responding (based on the PSA level and whether or not symptoms develop).

Remember that prostate cancer is usually slow growing, so even if it does come back, it may not cause problems for many years. In a Johns Hopkins University study of men whose PSA level began to rise after surgery, there was an average of about 8 years before there were signs the cancer had spread to distant parts of the body. Of course, these signs appeared earlier in some men and later in others.

## **Hormone-refractory Prostate Cancer (HRPC)**

Cancer that is no longer responding to hormone therapy such as LHRH analogs or anti-androgens is considered hormone-refractory, and can be hard to treat. At one time it was thought that chemotherapy was not effective against prostate cancer, but in recent years this notion has been challenged. Several chemotherapy drugs have been shown to reduce PSA levels and improve quality of life. Recent studies of chemotherapy regimens that include the

drug docetaxel have shown that it can improve survival by an average of several months, as well as reduce cancer pain.

Bisphosphonates appear to be helpful for many men whose cancer has spread to the bones. These drugs can reduce pain and even slow cancer growth in many cases. There are also other medicines and methods to keep pain and other symptoms under control. External radiation therapy can help treat bone pain if it is only in a few spots. Radioactive strontium or samarium may reduce pain if it is more widespread, and may also slow the growth of the cancer.

If you are having pain from your prostate cancer, make sure your doctor is aware of this. There are many very effective drugs that can relieve pain. But for this to happen, you must make it clear to your doctor that you have pain. For more information, see the American Cancer Society document, *Advanced Cancer*.

There are several promising new agents now being tested against prostate cancer, including vaccines, monoclonal antibodies, and differentiating agents. Because our ability to treat hormone-refractory prostate cancer is still not good enough, men are encouraged to explore new options by taking part in clinical trials.

## **More Treatment Information**

For more details on treatment options -- including some that may not be addressed in this document -- the National Comprehensive Cancer Network (NCCN) and the National Cancer Institute (NCI) are good sources of information.

The NCCN, made up of experts from many of the nation's leading cancer centers, develops cancer treatment guidelines for doctors. These are available on the NCCN Web site ([www.nccn.org](http://www.nccn.org)).

The American Cancer Society collaborates with the NCCN to produce a version of the prostate cancer treatment guidelines, written specifically for patients and their families. This less-technical version is available on both the NCCN Web site ([www.nccn.org](http://www.nccn.org)) and the ACS Web site ([www.cancer.org](http://www.cancer.org)). A print version can also be requested from the ACS at 1-800-ACS-2345.

The NCI provides treatment guidelines via its telephone information center (1-800-4-CANCER) and its Web site ([www.cancer.gov](http://www.cancer.gov)). Detailed guidelines intended for use by cancer care professionals are also available on [www.cancer.gov](http://www.cancer.gov).

## **What Should You Ask Your Doctor About Prostate Cancer?**

It is important for you to have honest, open discussions with your cancer care team. They want to answer all of your questions, no matter how minor you might think they are. For instance, consider asking these questions:

- What are the chances that the cancer has spread beyond my prostate? If so, is it still curable?

- What further tests (if any) do you recommend, and why?
- What is the clinical stage and Gleason score (grade) of my cancer? What do those mean in my case?
- What is my expected survival rate based on clinical stage, grade, and various treatment options?
- Should I consider watchful waiting as an option? Why or why not?
- Do you recommend a radical prostatectomy or radiation? Why or why not?
- If you recommend radical prostatectomy, will it be nerve sparing?
- Should I consider laparoscopic or robot-assisted prostatectomy?
- What types of radiation therapy might work best for me?
- What other treatment(s) might be right for me? Why?
- Among those treatments, what are the risks or side effects that I should expect?
- What are the chances that I will have problems with incontinence or impotence?
- What are the chances that I will have other urinary or rectal problems?
- What are the chances of recurrence of my cancer with the treatment programs we have discussed? What would be our next step if this happened?
- Should I follow a special diet?

In addition to these sample questions, be sure to write down some of your own. For instance, you might want to ask about recovery time so that you can plan your work schedule. If you are younger, you may want to discuss your plans for children if there is a possibility you could become impotent or sterile. You also may want to ask about second opinions or about clinical trials for which you may qualify.

## What Happens After Treatment for Prostate Cancer?

Completing treatment can be both stressful and exciting. You will be relieved to finish treatment, yet it is hard not to worry about cancer coming back. (When cancer returns, it is called recurrence.) This is a very common concern among those who have had cancer.

It may take a while before your confidence in your own recovery begins to feel real and your fears are somewhat relieved. Even with no recurrences, people who have had cancer learn to live with uncertainty.

## Follow-up Care

After treatment for prostate cancer, your doctor will want to watch you carefully, checking to see if your cancer recurs or spreads further. Your doctor should also outline a follow-up plan. This plan usually includes regular doctor visits, PSA blood tests, and digital rectal exams, which will likely begin within a few months of finishing treatment. Most doctors recommend PSA tests about every 6 months for the first 5 years after treatment, and at least yearly after that. Bone scans or other imaging tests may also be done, depending on your medical situation. This is the time for you to ask your health care team any questions you need answered and to discuss any concerns you might have.



Almost any cancer treatment can have side effects. Some may last for a few weeks to several months, but others can be permanent. Don't hesitate to tell your cancer care team about any symptoms or side effects that bother you so they can help you manage them.

It is also important to keep medical insurance. Even though no one wants to think of their cancer coming back, it is always a possibility. If it happens, the last thing you want is to have to worry about paying for treatment.

Prostate cancer can recur many years after initial treatment, which is why it is important to keep regular doctor visits and report any new symptoms (such as bone pain or problems with urination). Should your prostate cancer come back, your treatment options will depend on where it is thought to be located and what types of treatment you've already had. For more information, see the section, "How Is Prostate Cancer Treated?"

## Seeing a New Doctor

At some point after your cancer diagnosis and treatment, you may find yourself in the office of a new doctor. Your original doctor may have moved or retired, or you may have moved or changed doctors for some reason. It is important that you be able to give your new doctor the exact details of your diagnosis and treatment. Make sure you have the following information handy:

- a copy of your pathology report from any biopsy or surgery
- if you had surgery, a copy of your operative report
- if you were hospitalized, a copy of the discharge summary that every doctor must prepare when patients are sent home from the hospital
- finally, since some drugs can have long-term side effects, a list of your drugs, drug doses, and when you took them

## Lifestyle Changes to Consider During and After Treatment

Having cancer and dealing with treatment can be time-consuming and emotionally draining, but it can also be a time to look at your life in new ways. Maybe you are thinking about how to improve your health over the long term. Some people even begin this process during cancer treatment.

### Make Healthier Choices

Think about your life before you learned you had cancer. Were there things you did that might have made you less healthy? Maybe you drank too much alcohol, or ate more than you needed, or smoked, or didn't exercise very often. Emotionally, maybe you kept your feelings bottled up, or maybe you let stressful situations go on too long.

Now is not the time to feel guilty or to blame yourself. However, you can start making changes *today* that can have positive effects for the rest of your life. Not only will you feel better but you will also be healthier. What better time than now to take advantage of the motivation you have as a result of going through a life-changing experience like having cancer?

You can start by working on those things that you feel most concerned about. Get help with those that are harder for you. For instance, if you are thinking about quitting smoking and need help, call the American Cancer Society's Quitline® tobacco cessation program at 1-800-ACS-2345.

### **Diet and Nutrition**

Eating right can be a challenge for anyone, but it can get even tougher during and after cancer treatment. For instance, treatment often may change your sense of taste. Nausea can be a problem. You may lose your appetite for a while and lose weight when you don't want to. On the other hand, some people gain weight even without eating more. This can be frustrating, too.

If you are losing weight or have taste problems during treatment, do the best you can with eating and remember that these problems usually improve over time. You may want to ask your cancer team for a referral to a dietitian, an expert in nutrition who can give you ideas on how to fight some of the side effects of your treatment. You may also find it helps to eat small portions every 2 to 3 hours until you feel better and can go back to a more normal schedule.

One of the best things you can do after treatment is to put healthy eating habits into place. You will be surprised at the long-term benefits of some simple changes, like increasing the variety of healthy foods you eat. Try to eat 5 or more servings of vegetables and fruits each day. Choose whole grain foods instead of white flour and sugars. Try to limit meats that are high in fat. Cut back on processed meats like hot dogs, bologna, and bacon. Get rid of them altogether if you can. If you drink alcohol, limit yourself to 1 or 2 drinks a day at the most. And don't forget to get some type of regular exercise. The combination of a good diet and regular exercise will help you maintain a healthy weight and keep you feeling more energetic.

### **Rest, Fatigue, Work, and Exercise**

Fatigue is a very common symptom in people being treated for cancer. This is often not an ordinary type of tiredness but a "bone-weary" exhaustion that doesn't get better with rest. For some, this fatigue lasts a long time after treatment, and can discourage them from physical activity.

However, exercise can actually help you reduce fatigue. Studies have shown that patients who follow an exercise program tailored to their personal needs feel physically and emotionally improved and can cope better.

If you are ill and need to be on bed rest during treatment, it is normal to expect your fitness, endurance, and muscle strength to decline some. Physical therapy can help you maintain strength and range of motion in your muscles, which can help fight fatigue and the sense of depression that sometimes comes with feeling so tired.

Any program of physical activity should fit your own situation. An older person who has never exercised will not be able to take on the same amount of exercise as a 20-year-old who plays tennis 3 times a week. If you haven't exercised in a few years but can still get around, you may want to think about taking short walks.

Talk with your health care team before starting, and get their opinion about your exercise plans. Then, try to get an exercise buddy so that you're not doing it alone. Having family or friends involved when starting a new exercise program can give you that extra boost of support to keep you going when the push just isn't there.

If you are very tired, though, you will need to balance activity with rest. It is okay to rest when you need to. It is really hard for some people to allow themselves to do that when they are used to working all day or taking care of a household. (For more information about fatigue, please see the publication, *Cancer-Related Fatigue and Anemia Treatment Guidelines for Patients*.)

Exercise can improve your physical and emotional health.

- It improves your cardiovascular (heart and circulation) fitness.
- It strengthens your muscles.
- It reduces fatigue.
- It lowers anxiety and depression.
- It makes you feel generally happier.
- It helps you feel better about yourself.

And long term, we know that exercise plays a role in preventing some cancers. The American Cancer Society, in its guidelines on physical activity for cancer prevention, recommends that adults take part in at least 30 minutes of moderate to vigorous physical activity, above usual activities, on 5 or more days of the week; 45 to 60 minutes of intentional physical activity are preferable.

## **How About Your Emotional Health?**

Once your treatment ends, you may find yourself overwhelmed by emotions. This happens to a lot of people. You may have been going through so much during treatment that you could only focus on getting through your treatment.

Now you may find that you think about the potential of your own death, or the effect of your cancer on your family, friends, and career. You may also begin to re-evaluate your relationship with your spouse or partner. Unexpected issues may also cause concern -- for instance, as you become healthier and have fewer doctor visits, you will see your health care team less often. That can be a source of anxiety for some.

This is an ideal time to seek out emotional and social support. You need people you can turn to for strength and comfort. Support can come in many forms: family, friends, cancer support groups, church or spiritual groups, online support communities, or individual counselors.

Almost everyone who has been through cancer can benefit from getting some type of support. What's best for you depends on your situation and personality. Some people feel safe in peer-support groups or education groups. Others would rather talk in an informal setting, such as church. Others may feel more at ease talking one-on-one with a trusted friend or counselor. Whatever your source of strength or comfort, make sure you have a place to go with your concerns.

The cancer journey can feel very lonely. It is not necessary or realistic to go it all by yourself. And your friends and family may feel shut out if you decide not to include them. Let them in -- and let in anyone else who you feel may help. If you aren't sure who can help, call your American Cancer Society at 1-800-ACS-2345 and we can put you in touch with an appropriate group or resource.

You can't change the fact that you have had cancer. What you can change is how you live the rest of your life -- making healthy choices and feeling as well as possible, physically and emotionally.

### **What Happens if Treatment Is No Longer Working?**

If cancer continues to grow after one kind of treatment, or if it returns, it is often possible to try another treatment plan that might still cure the cancer, or at least shrink the tumors enough to help you live longer and feel better. On the other hand, when a person has received several different medical treatments and the cancer has not been cured, over time the cancer tends to become resistant to all treatment. At this time it's important to weigh the possible limited benefit of a new treatment against the possible downsides, including continued doctor visits and treatment side effects.

Everyone has his or her own way of looking at this. Some people may want to focus on remaining comfortable during their limited time left.

This is likely to be the most difficult time in your battle with cancer -- when you have tried everything medically within reason and it's just not working anymore. Although your doctor may offer you new treatment, you need to consider that at some point, continuing treatment is not likely to improve your health or change your prognosis or survival.

If you want to continue treatment to fight your cancer as long as you can, you still need to consider the odds of more treatment having any benefit. In many cases, your doctor can estimate the response rate for the treatment you are considering. Some people are tempted to try more chemotherapy or radiation, for example, even when their doctors say that the odds of benefit are less than 1%. In this situation, you need to think about and understand your reasons for choosing this plan.

No matter what you decide to do, it is important that you be as comfortable as possible. Make sure you are asking for and getting treatment for any symptoms you might have, such as pain. This type of treatment is called *palliative* treatment.

Palliative treatment helps relieve symptoms, but is not expected to cure the disease; its main purpose is to improve your quality of life. Sometimes, the treatments you get to control your symptoms are similar to the treatments used to treat cancer. For example, radiation therapy might be given to help relieve bone pain from bone metastasis. Or chemotherapy might be given to help shrink a tumor and keep it from causing a bowel obstruction. But this is not the same as receiving treatment to try to cure the cancer.

At some point, you may benefit from hospice care. Most of the time, this can be given at home. Your cancer may be causing symptoms or problems that need attention, and hospice focuses on your comfort. You should know that receiving hospice care doesn't mean you can't have treatment for the problems caused by your cancer or other health conditions. It just means that the focus of your care is on living life as fully as possible and feeling as well as you can at this difficult stage of your cancer.

Remember also that maintaining hope is important. Your hope for a cure may not be as bright, but there is still hope for good times with family and friends -- times that are filled with happiness and meaning. In a way, pausing at this time in your cancer treatment is an opportunity to refocus on the most important things in your life. This is the time to do some things you've always wanted to do and to stop doing the things you no longer want to do.

## What's New in Prostate Cancer Research and Treatment?

Research into the causes, prevention, and treatment of prostate is under way in many medical centers throughout the world.

### Genetics

New research on genes linked to prostate cancer is helping scientists better understand how prostate cancer develops. These studies are expected to provide answers about the genetic changes that lead to prostate cancer. This could make it possible to design medicines to reverse those changes. Tests to find abnormal prostate cancer genes could also help identify men at high risk who would benefit from more intensive screening or from chemoprevention trials, which use drugs to try to keep them from getting cancer.

Most of the genes that have been studied so far are from chromosomes that are inherited from both parents. One recent study found that a certain variant of mitochondrial DNA, which is inherited only from a person's mother, might double or even triple a man's risk of developing prostate cancer.

An exciting new development in genetics research is the use of *DNA microarray* technology which allows scientists to study thousands of genes at the same time. Using this method, researchers have identified several genes now thought to play a role in prostate cancer. This may eventually provide more sensitive screening tests for prostate cancer than the PSA blood test currently in use.

One of the biggest problems now facing men with prostate cancer and their doctors is figuring out which cancers are likely to stay within the gland and which are more likely to

grow and spread (and definitely need treatment). New discoveries may help with this some time in the near future. For example, the product of one gene identified by DNA microarray, known as EZH2, seems to appear more often in advanced prostate cancers than in those at an early stage. Researchers are now trying to decide whether the presence of this gene product, or others, indicates that a cancer is more aggressive. This could eventually help tell which men need treatment and which might be better served by watchful waiting.

## **Prevention**

Researchers continue to look for foods that increase or decrease prostate cancer risk. Scientists have found some substances in tomatoes (lycopenes) and soybeans (isoflavones) that may help prevent prostate cancer. Studies are now looking at the possible effects of these compounds more closely. Scientists are also trying to develop related compounds that are even more potent and might be used as dietary supplements. So far, most research suggests that a balanced diet including these foods as well as other fruits and vegetables is of greater benefit than taking these substances as dietary supplements.

Some studies suggest that certain vitamin and mineral supplements (such as vitamin E and selenium) may lower prostate cancer risk. A large study of this issue, called the Selenium and Vitamin E Cancer Prevention Trial (SELECT), is still in progress. Another vitamin that may be important is vitamin D. Recent studies have found that men with high levels of vitamin D seem to have a lower risk of developing the more lethal forms of prostate cancer.

Although many people assume that vitamins are natural substances that cause no harm, recent research has shown that high doses may be harmful. One study found that men who take more than 7 multivitamin tablets per week may have an increased risk of developing advanced prostate cancer.

Scientists are also testing certain hormonal medicines as a way of reducing prostate cancer risk. Finasteride (Proscar) and dutasteride (Avodart) are drugs that lower the body's levels of a potent androgen called DHT. Both drugs are already used to treat benign prostatic hyperplasia (BPH). The results of one such study, the Prostate Cancer Prevention Trial are discussed above in the section, "Can Prostate Cancer Be Prevented?" This study looked at the possible benefits of finasteride, although the results were not clear-cut. Another study is looking at whether dutasteride might be helpful in reducing the risk of getting prostate cancer.

## **Early Detection**

Doctors agree that the PSA blood test is not a perfect test for finding prostate cancer early. It misses some cancers, and in other cases it is elevated when cancer isn't present. Researchers are working on two strategies to address this problem.

One approach is to try to improve on the test that measures the total PSA level, as described in the section, "Can Prostate Cancer Be Found Early?" The percent-free PSA is one way to do this, although it requires two separate tests. Another option might be to measure only the "complexed" PSA (the portion of PSA that is not "free") to begin with, instead of the total

and free PSA. This one test could give the same amount of information as the other two done separately. Studies are now under way to see if this test provides the same level of accuracy.

The other approach is to develop new tests based on other tumor markers. Several newer blood tests seem to be more accurate than the PSA test, based on early studies. One example is a blood test for a marker called EPCA-2. Another approach is to look for signs of the body's own immune reaction to substances made by prostate cancer cells. While early results have been promising, these and other new tests are not yet available outside of research labs and will require more study before they are widely used to test for prostate cancer.

## Diagnosis

Doctors performing prostate biopsies often rely on transrectal ultrasound (TRUS), which creates black and white images of the prostate using sound waves, to know where to take samples from. But standard ultrasound may not detect some areas containing cancer. A fairly new technique, known as *color Doppler ultrasound*, measures blood flow within the gland. (Tumors often have more blood vessels around them than normal tissue.) It may make prostate biopsies more accurate by helping to ensure the right part of the gland is sampled. An even newer technique may enhance color Doppler further. It involves first injecting the patient with a contrast agent containing microbubbles. Promising results have been reported, but more studies will be needed before its use becomes common.

## Staging

Staging plays a key role in deciding which treatment options a man may be eligible for. But imaging tests for prostate cancer such as CT and MRI scans can't detect all cancers, especially small areas of cancer in lymph nodes. A newer method, called *enhanced MRI*, may help find lymph nodes that contain cancer. Patients first have a standard MRI. They are then injected with tiny magnetic particles and have another scan done the next day. Differences between the 2 scans point to possible cancer cells in the lymph nodes. Early results of this technique are promising, but it needs more research before it becomes widely used.

## Treatment

This is a very active area of research. Newer treatments are being developed, and improvements are being made among many standard prostate cancer treatment methods.

### Surgery

If the nerves that control erections (which run along either side of the prostate) must be removed during the operation, a man will become impotent. Some doctors are now exploring the use of *sural nerve grafts* to try to restore potency if the original nerves must be removed. This approach, done at the same time as the radical prostatectomy, involves replacing the original nerves with small nerves taken from the side of the foot. This is still considered an experimental technique, and not all doctors agree as to its usefulness. Further study is under way.

### Radiation Therapy

As described in the section, "How Is Prostate Cancer Treated?" advances in technology are making it possible to aim radiation more precisely than in the past. Currently used methods such as conformal radiation therapy (CRT) and intensity modulated radiation therapy (IMRT) allow doctors to treat only the prostate gland and avoid radiation to normal tissues as much as possible. This is expected to increase the effectiveness and reduce the side effects of radiation therapy. Studies are being done to find out which radiation techniques are best suited for specific groups of patients with prostate cancer.

Newer forms of radiation therapy that deliver radiation from several angles, such as the CyberKnife and helical tomotherapy, may provide even more precise delivery of radiation to the prostate while sparing normal tissues. These newer approaches have only been available for a short time, so there is limited data on them.

Technology is making other forms of radiation therapy more effective as well. New computer programs allow doctors to better plan the radiation doses and approaches for both external radiation therapy and brachytherapy. Planning for brachytherapy can now even be done during the procedure (intraoperatively).

### **Newer Treatments for Localized Disease**

Researchers are looking at newer forms of treatment for early stage prostate cancer. These new treatments could be used either as the first type of treatment or be used after radiation therapy in cases where it was not successful.

One promising treatment, known as *high-intensity focused ultrasound (HIFU)*, destroys cancer cells by heating them with highly focused ultrasonic beams. While it has been used more in Europe, it is not commonly employed in the United States at this time. Studies are now under way to determine its safety and effectiveness.

### **Nutrition and Lifestyle Changes**

A recent study found that in men with a rising PSA after surgery or radiation therapy, drinking pomegranate juice seemed to slow the time it took the PSA level to double. Larger studies are now under way to try to confirm these results.

Some encouraging early results have also been reported with flaxseed supplements. One small study in men with early prostate cancer found that daily flaxseed seemed to slow the rate at which prostate cancer cells multiplied. More research is needed to confirm this finding.

A recent report found that men who chose not to have treatment for their localized prostate cancer may be able to slow its growth with intensive lifestyle changes. The men ate a vegan (no meat, fish, eggs, or dairy products) diet and exercised frequently. They also took part in support groups and yoga. After one year the men saw, on average, a slight drop in their PSA level. It isn't known whether this effect will last since the report only followed the men for 1 year. The regimen may also be hard to follow for some men.



## **Chemotherapy**

Studies in recent years have shown that many chemotherapy drugs can affect prostate cancer. At least one drug (docetaxel) has been shown to help men live longer. Several new chemotherapy drugs and combinations of drugs are now being studied.

One newer drug is satraplatin, which is in late-stage clinical trials as a second-line chemotherapy option for men with advanced, hormone-refractory prostate cancer. Satraplatin is taken as a pill. It is now being looked at by the FDA for possible approval.

Calcitriol, a form of vitamin D, has recently shown promising results when combined with docetaxel (Taxotere). Men who received the combination seemed to do better than men in other studies who received only docetaxel. A large clinical trial is now comparing a high-dose form of calcitriol (DN-101) and docetaxel to docetaxel alone.

## **Prostate Cancer Vaccines**

Several types of vaccines for boosting the body's immune response to prostate cancer cells are being tested in clinical trials. Unlike vaccines against infections like measles or mumps, these vaccines are designed to help treat, not prevent, prostate cancer. One possible advantage of these types of treatments is that they seem to have very limited side effects. At this time, vaccines are only available in clinical trials.

The furthest along in terms of development is sipuleucel-T (Provenge). For this vaccine, dendritic cells (cells of the immune system) are removed from the patient's blood and exposed to a part of prostate cancer cells called prostatic acid phosphatase (PAP). These cells are then put back into the body where they induce other immune system cells to attack the patient's prostate cancer. A small study found that the vaccine seemed to increase survival in men with advanced, hormone-refractory prostate cancer, and further studies are under way. Provenge is now being looked at by the FDA for possible approval.

A vaccine known as GVAX has also shown promise against advanced, hormone-refractory prostate cancer in early studies. This vaccine is made up of prostate cancer cells that have been genetically modified to make GM-CSF, a substance that boosts the immune response against them. GVAX is now in late-stage clinical trials.

Another prostate cancer vaccine (PROSTVAC-VF) uses a virus that has been genetically modified to contain prostate-specific antigen (PSA). The patient's immune system should respond to the virus and begin to recognize and destroy cancer cells containing PSA. This vaccine is still in early-stage clinical trials.

Several other prostate cancer vaccines are also in development.

## **Monoclonal Antibodies**

Monoclonal antibodies are manmade versions of immune system proteins designed to target specific molecules in prostate cancer cells. Several different ones are being developed and tested.

For example, pertuzumab is a monoclonal antibody directed against the HER2 protein, which is sometimes found in excess amounts on the surface of cancer cells. Studies of men with advanced, hormone-refractory prostate cancer have not found that pertuzumab shrinks tumors or lowers PSA levels, although one study found it may have helped men live longer than would be expected.

### **Angiogenesis Inhibitors**

Growth of prostate cancer tumors depends on growth of blood vessels (angiogenesis) to nourish the cancer cells. Looking at angiogenesis in prostate cancer specimens may help predict treatment outcomes. Cancers that stimulate many new vessels to grow are harder to treat and have a poorer outlook.

New drugs are being studied that may be useful in stopping prostate cancer growth by keeping new blood vessels from forming. Several anti-angiogenic drugs are already being tested in clinical trials. One of these is thalidomide, which has been approved by the FDA to treat patients with multiple myeloma. It is being combined with chemotherapy in clinical trials to treat men with advanced prostate cancer. While promising, this drug can cause major side effects, including constipation, drowsiness, and nerve damage.

Another drug, bevacizumab (Avastin), is FDA-approved to treat patients with other cancers. It is now being tested in combination with hormone therapy and chemotherapy in men with advanced prostate cancer.

### **Treatment of Bone Pain**

Doctors are now studying the use of *radiofrequency ablation (RFA)* to help control pain in men whose prostate cancer has spread to one or more areas in the bones. During RFA, the doctor uses computed tomography (CT) or ultrasound to guide a small metal probe into the area of the tumor. A high frequency current passed through the probe heats and destroys the tumor. While RFA has been used for many years to treat tumors in other organs such as the liver, its use in treating bone pain is still fairly new.

## **Additional Resources**

### **More Information From Your American Cancer Society**

The following information may also be helpful to you. These materials may be viewed on our Web site or ordered from our toll-free number, 1-800-ACS-2345.

Caring for the Person With Cancer at Home: A Guide for Patients and Families (also available in Spanish)

Guidelines for the Early Detection of Cancer (also available in Spanish)

Managing Incontinence After Treatment For Prostate Cancer

Prostate Cancer: Treatment Guidelines for Patients (also available in Spanish)

Sexuality and Cancer: For the Man Who Has Cancer and His Partner (also available in Spanish)

**The following books are available from the American Cancer Society. Call us at 1-800-ACS-2345 to ask about costs or to place your order.**

*American Cancer Society's Complete Guide to Prostate Cancer*

*American Cancer Society's Guide to Pain Control: Understanding and Managing Cancer Pain*

*Cancer in the Family: Helping Children Cope With a Parent's Illness*

*Caregiving: A Step-By-Step Resource for Caring for the Person With Cancer at Home*

*Consumers Guide to Cancer Drugs*, 2nd edition

*Informed Decisions: The Complete Book of Cancer Diagnosis, Treatment, and Recovery*, Second Edition

## **National Organizations and Web Sites\***

In addition to the American Cancer Society, other sources of patient information and support include:

American Urological Association Foundation  
Telephone: 1-866-746-4282 (1-866-RING-AUA)  
Internet Address: [www.urologyhealth.org](http://www.urologyhealth.org)

National Association for Continence  
Telephone: 1-800-252-3337 (1-800-BLADDER)  
Internet Address: [www.nafc.org](http://www.nafc.org)

National Cancer Institute  
Telephone: 1-800-422-6237 (1-800-4-CANCER); TTY: 1-800-332-8615  
Internet Address: [www.cancer.gov](http://www.cancer.gov)

National Coalition for Cancer Survivorship  
Telephone: 1-877-622-7937 (1-877-NCCS-YES)  
Internet Address: [www.canceradvocacy.org](http://www.canceradvocacy.org)

National Prostate Cancer Coalition  
Telephone: 1-888-245-9455  
Internet Address: [www.fightprostatecancer.org](http://www.fightprostatecancer.org)

Prostate Cancer Foundation (formerly "CaPCURE")  
Telephone: 1-800-757-2873 (1-800-757-CURE) or 1-310-570-4700  
Internet Address: [www.prostatecancerfoundation.org](http://www.prostatecancerfoundation.org)

US Too International, Inc.  
Telephone: 1-800-808-7866 (1-800-80US TOO) or 1-630-795-1002 (Chicago area)  
Internet Address: [www.ustoo.com](http://www.ustoo.com)

*\* Inclusion on this list does not imply endorsement by the American Cancer Society.*

The American Cancer Society is happy to address almost any cancer-related topic. If you have any more questions, please call us at 1-800-ACS-2345 any time, 24 hours a day.

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