Prostate Cancer

What is cancer?

The body is made up of trillions of living cells. Normal body cells grow, divide into new cells, and die in an orderly way. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of out-of-control growth of abnormal cells.

Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. Cancer cells can also invade (grow into) other tissues, something that normal cells cannot do. Growing out of control and invading other tissues are what makes a cell a cancer cell.

Cells become cancer cells because of damage to DNA. DNA is in every cell and directs all its actions. In a normal cell, when DNA gets damaged the cell either repairs the damage or the cell dies. In cancer cells, the damaged DNA is not repaired, but the cell doesn’t die like it should. Instead, this cell goes on making new cells that the body does not need. These new cells will all have the same damaged DNA as the first cell does.

People can inherit damaged DNA, but most DNA damage is caused by mistakes that happen while the normal cell is reproducing or by something in our environment. Sometimes the cause of the DNA damage is something obvious, like cigarette smoking. But often no clear cause is found.

In most cases the cancer cells form a tumor. Some cancers, like leukemia, rarely form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

Cancer cells often travel to other parts of the body, where they begin to grow and form new tumors that replace normal tissue. This process is called *metastasis*. It happens when the cancer cells get into the bloodstream or lymph vessels of our body.

No matter where a cancer may spread, it is always named for the place where it started. For example, breast cancer that has spread to the liver is still called breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bone is metastatic prostate cancer, not bone cancer.

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.

Not all tumors are cancerous. Tumors that aren't cancer are called *benign*. Benign tumors can cause problems – they can grow very large and press on healthy organs and tissues. But they cannot grow into (invade) other tissues. Because they can't invade, they also can't spread to other parts of the body (metastasize). These tumors are almost never life threatening.

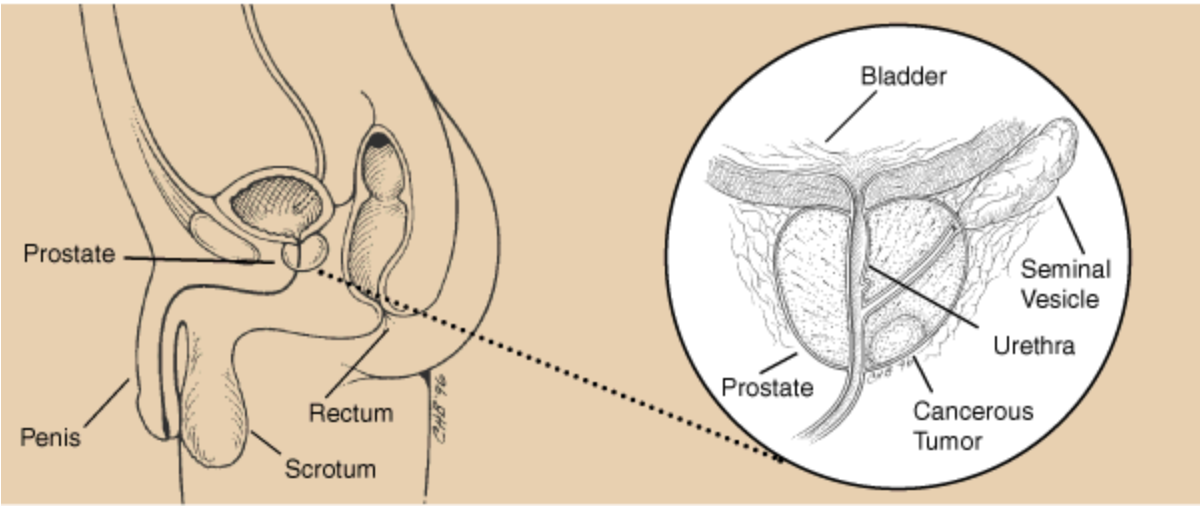
What is prostate cancer?

To understand prostate cancer, it helps to know something about the prostate and nearby structures in the body.

About the prostate

The prostate is a gland found only in males. It is located in front of the rectum and below the urinary bladder. The size of the prostate varies with age. In younger men, it is about the size of a walnut, but it can be much larger in older men.

The prostate's job is to make some of the fluid that protects and nourishes sperm cells in semen, making the semen more liquid. Just behind the prostate are glands called *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, goes through the center of the prostate.



The prostate starts to develop before birth. It grows rapidly during puberty, fueled by male hormones (called *androgens*) in the body. The main androgen, *testosterone*, is made in the testicles. The enzyme *5-alpha reductase* converts testosterone into *dihydrotestosterone* (DHT). DHT is the main hormone that signals the prostate to grow.

The prostate usually stays at about the same size or grows slowly in adults, as long as male hormones are present.

Benign prostatic hyperplasia

The inner part of the prostate (around the urethra) often keeps growing as men get older, which can lead to a common condition called *benign prostatic hyperplasia* (BPH). In BPH, the prostate tissue can press on the urethra, leading to problems passing urine.

BPH is *not* cancer and does not develop into cancer. But it can be a serious medical problem for some men. If it requires treatment, medicines can often be used to shrink the size of the prostate or to relax the muscles in it, which usually helps with urine flow. If medicines aren't helpful, some type of surgery, such as a transurethral resection of the prostate (TURP) may be needed. (See the "Surgery for prostate cancer" section for a description of this procedure.)

Prostate cancer

Several types of cells are found in the prostate, but almost all 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 these types of prostate cancer are so

rare that if you have prostate cancer it is almost certain to be an adenocarcinoma. **The rest of this document refers only to prostate adenocarcinoma.**

Some prostate cancers can grow and spread quickly, but most 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 many cases neither they nor their doctors even knew they had it.

Possible pre-cancerous conditions of the prostate

Some doctors believe that prostate cancer starts out as a pre-cancerous condition, although this is not yet known for sure.

Prostatic intraepithelial neoplasia (PIN)

In this condition, there are changes in how the prostate gland cells look under the microscope, but the abnormal cells don't look like they are growing into other parts of the prostate (like cancer cells would). Based on how abnormal the patterns of cells look, they are classified as:

- **Low-grade PIN:** the patterns of prostate cells appear almost normal
- **High-grade PIN:** the patterns of cells look more abnormal

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. Many men begin to develop low-grade PIN at an early age but do not necessarily develop prostate cancer. The importance of low-grade PIN in relation to prostate cancer is still unclear. If a finding of low-grade PIN is reported on a prostate biopsy, the follow-up for patients is usually the same as if nothing abnormal was seen.

If high-grade PIN has been found on your prostate biopsy, there is about a 20% to 30% chance that you also have cancer in another area of your prostate. This is why doctors often watch men with high-grade PIN carefully and may advise them to have a repeat prostate biopsy, especially if the original biopsy did not take samples from all parts of the prostate.

Proliferative inflammatory atrophy (PIA)

This is another finding that may be noted on a prostate biopsy. In PIA, the prostate cells look smaller than normal, and there are signs of inflammation in the area. PIA is not cancer, but researchers believe that PIA may sometimes lead to high-grade PIN, or perhaps to prostate cancer directly.

What are the key statistics about prostate cancer?

Other than skin cancer, prostate cancer is the most common cancer in American men. The American Cancer Society’s estimates for prostate cancer in the United States for 2014 are:

- About 233,000 new cases of prostate cancer will be diagnosed
- About 29,480 men will die of prostate cancer

About 1 man in 7 will be diagnosed with prostate cancer during his lifetime.

Prostate cancer occurs mainly in older men. About 6 cases in 10 are diagnosed in men aged 65 or older, and it is rare before age 40. The average age at the time of diagnosis is about 66.

Prostate cancer is the second leading cause of cancer death in American men, behind only lung cancer. About 1 man in 36 will die of prostate cancer.

Prostate cancer can be a serious disease, but most men diagnosed with prostate cancer do not die from it. In fact, more than 2.5 million men in the United States who have been diagnosed with prostate cancer at some point are still alive today.

For statistics related to survival, see the section "Survival rates for prostate cancer."

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. Some risk factors, like smoking, can be changed. Others, like a person's age or family history, can't be changed.

But risk factors don't tell us everything. Many people with one or more risk factors never get cancer, while others who get cancer may have had few or no known risk factors.

We don't yet completely understand the causes of prostate cancer, but researchers have found several factors that might change the risk of getting it. For some of these factors, the link to prostate cancer risk is not yet clear.

Age

Prostate cancer is very rare in men younger than 40, but the chance of having prostate cancer rises rapidly after age 50. About 6 in 10 cases of prostate cancer are found in men over the age of 65.

Race/ethnicity

Prostate cancer occurs more often in African-American men and Caribbean men of African ancestry 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 probably accounts for at least part of this difference, but other factors such as lifestyle differences (diet, etc.) are likely to be important as well. For example, 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 who have a brother with the disease 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.

Genes

Scientists have found several inherited gene changes that seem to raise prostate cancer risk, but they probably account for only a small number of cases overall. Genetic testing for most of these gene changes is not yet available.

Some inherited gene changes 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. Mutations in these genes may also increase prostate cancer risk in some men, but they account for a very small percentage of prostate cancer cases.

Recently, some common gene variations have been linked to a higher risk of prostate cancer. Studies to confirm this are needed to see if testing for the gene variants will be useful in predicting prostate cancer risk.

For more on some of the gene changes linked to prostate cancer, see “Do we know what causes prostate cancer?”

Diet

The exact role of diet in prostate cancer is not clear, but several 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 prostate cancer. Dairy foods (which are often high in calcium) might also increase risk. 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.

Obesity

Most studies have not found that being obese (very overweight) is linked with a higher risk of getting prostate cancer overall.

Some studies have found that obese men have a lower risk of getting a low-grade (less dangerous) form of the disease, but a higher risk of getting more aggressive prostate cancer. The reasons for this are not clear.

Some studies have also found that obese men may be at greater risk for having more advanced prostate cancer and of dying from prostate cancer, but not all studies have found this.

Smoking

Most studies have not found a link between smoking and the risk of developing prostate cancer. Some recent research has linked smoking to a possible small increase in the risk

of death from prostate cancer, but this is a new finding that will need to be confirmed by other studies.

Workplace exposures

There is some evidence that firefighters are exposed to substances (toxic combustion products) that may increase risk.

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, but other studies have not found such a link. Inflammation is often seen in samples of prostate tissue that also contain cancer. The link between the two is not yet clear, but this is an active area of research.

Sexually transmitted infections

Researchers have looked to see if sexually transmitted infections (like gonorrhea or chlamydia) might increase the risk of prostate cancer, possibly because they may lead to inflammation of the prostate. So far, studies have not agreed, and no firm conclusions have been reached.

Vasectomy

Some earlier studies had suggested that men who have 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 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 cell. In recent 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 makes up our genes, the instructions for nearly everything our cells do. We usually look like our parents because they are the source of our DNA. However, DNA affects more than how we look.

Some genes control when our cells grow, divide into new cells, and die. Certain genes that tell cells to grow and divide are called *oncogene*s. 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 in part 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 that 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 Gene **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.

Men with *BRCA1* or *BRCA2* gene changes may also have an increased prostate cancer risk. Mutations in these genes more commonly cause breast and ovarian cancer in women. But inherited *BRCA* changes probably account for 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 flawed DNA in the new cell.

It is not clear how often these DNA changes might be random events, and how often they 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 is similar to insulin, but it affects 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 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?

The exact cause of prostate cancer is not known, so 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, there are some things you can do that might lower your risk of prostate cancer.

Body weight, physical activity, and diet

The effects of body weight, physical activity, and diet on prostate cancer risk are not clear, but there may be things you can do that might lower your risk.

Some studies have found that men who are overweight may have a slightly lower risk of prostate cancer overall, but a higher risk of prostate cancers that are likely to be fatal.

Studies have found that men who get regular physical activity have a slightly lower risk of prostate cancer. Vigorous activity may have a greater effect, especially on the risk of advanced prostate cancer.

Several studies have suggested that diets high in certain vegetables (including tomatoes, cruciferous vegetables, soy, beans, and other legumes) or fish may be linked with a lower risk of prostate cancer, especially more advanced cancers. Examples of cruciferous vegetables include cabbage, broccoli, and cauliflower.

Although not all studies agree, several have found a higher risk of prostate cancer in men who have diets high in calcium. There may also be an increased risk from consuming dairy foods.

For now, the best advice about diet and activity to possibly reduce the risk of prostate cancer is to:

- Eat at least 2½ cups of a wide variety of vegetables and fruits each day.
- Be physically active.

- Stay at a healthy weight.

It may also be sensible to limit calcium supplements and to not get too much calcium in the diet. (This does not mean that men who are being *treated for* prostate cancer should not take calcium supplements if their doctor recommends them.)

For more information, see the *American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention*.

Vitamin, mineral, and other supplements

Some earlier studies suggested that taking certain vitamin or mineral supplements might lower prostate cancer risk. Of special interest were vitamin E and the mineral selenium.

To study the possible effects of selenium and vitamin E on prostate cancer risk, doctors conducted the Selenium and Vitamin E Cancer Prevention Trial (SELECT). Men in this large study took one or both of these supplements or an inactive placebo each day for about 5 years. Neither vitamin E nor selenium was found to lower prostate cancer risk in this study. In fact, men taking the vitamin E supplements were later found to have a slightly higher risk of prostate cancer. For selenium supplements, the risk of prostate cancer was unchanged in men who had lower selenium levels at the start of the study. Men who had higher baseline levels, though, had an increased risk of high-grade (fast growing) prostate cancer.

Taking any supplements can have both risks and benefits. Before starting vitamins or other supplements, talk with your doctor.

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 help reduce the risk of prostate cancer.

5-alpha reductase inhibitors

5-alpha reductase is the enzyme in the body that changes testosterone into dihydrotestosterone (DHT), the main hormone that causes the prostate to grow. Drugs called 5-alpha reductase inhibitors block the enzyme and prevent the formation of DHT.

Two 5-alpha reductase inhibitors are already in use to treat benign prostatic hyperplasia (BPH), a non-cancerous growth of the prostate:

- Finasteride (Proscar®)
- Dutasteride (Avodart®)

Large studies of both of these drugs have been done to see if they might also be useful in lowering prostate cancer risk. In these studies, men taking either drug were less likely to develop prostate cancer after several years than men getting an inactive placebo.

When the results were looked at more closely, the men who took these drugs had fewer cases of prostate cancers that were low-grade, but slightly more cases of prostate cancer that were intermediate or high-grade. The grade of a cancer is based on how it looks under the microscope. Intermediate and high-grade cancers are more likely to grow and spread than low-grade cancers. Over the long term, though, this didn’t seem to affect death rates - both groups of men had similar survival.

These drugs can cause sexual side effects like lowered sexual desire and impotence. But they can help with problems from BPH such as trouble urinating.

Although these drugs are safe, they aren’t approved by the FDA to prevent prostate cancer. Right now, it isn’t clear that taking finasteride or dutasteride just to lower prostate cancer risk is very helpful. Still, men who want to know more about these drugs should discuss them with their doctors.

Other drugs

Other drugs and dietary supplements that may help lower prostate cancer risk are now being tested in clinical trials. No other drug or supplement has been found to be helpful in studies large enough to allow experts to recommend they should be given to men.

Can prostate cancer be found early?

Screening refers to testing to find a disease such as cancer in people who do not have symptoms of that disease. For some types of cancer, screening can help find cancers at an early stage, when they are more easily cured.

Prostate cancer can often be found early by testing the amount of prostate-specific antigen (PSA) in a man's blood. Another way to find prostate cancer is the digital rectal exam (DRE), in which the doctor puts a gloved finger into the rectum to feel the prostate gland. These 2 tests are described later on in more detail.

If the results of either one of these tests are abnormal, further testing is needed to see if there is a cancer. If prostate cancer is found as a result of screening with the PSA test or DRE, it will probably be at an earlier, more treatable stage than if no screening were done.

Since the use of early detection tests for prostate cancer became fairly common in the United States (about 1990), the prostate cancer death rate has dropped. But it isn't yet clear if this drop is a direct result of screening or if it might be caused by something else, like improvements in treatment.

There is no question that screening can help find many prostate cancers early, but there are limits to the prostate cancer screening tests used today. Neither the PSA test nor the DRE is 100% accurate. These tests can sometimes have abnormal results even when a man does not have cancer (known as *false positive* results). Normal results can also occur even when a man does have cancer (known as *false negative* results). Unclear test results can cause confusion and anxiety. False-positive results can lead some men to have a prostate biopsy (with small risks of pain, infection, and bleeding) when they do not have cancer. And false-negative results can give some men a false sense of security even though they actually have cancer.

Another important issue is that even if screening detects a cancer, doctors often can't tell if the cancer is truly dangerous. Finding and treating all prostate cancers early might seem as if it would always be a good thing. But some prostate cancers grow so slowly that they would probably never cause problems. Because of an elevated PSA level, some men may be diagnosed with a prostate cancer that they would have never even known about at all. It would never have lead to their death, or even caused any symptoms.

But these men may still be treated with either surgery or radiation, either because the doctor can't be sure how quickly the cancer might grow and spread, or because the men are uncomfortable knowing they have cancer and not getting any treatment. Treatments like surgery and radiation can have urinary, bowel, and/or sexual side effects that may seriously affect a man's quality of life.

Men and their doctors may end up struggling over whether they need treatment or whether they might be able to be followed without being treated right away (an approach called *watchful waiting* or *active surveillance*). Even when men are not treated right away, they still need regular blood tests and prostate biopsies to determine the need for future treatment. These tests are linked with risks of anxiety, pain, infection, and bleeding.

To help figure out if prostate cancer screening is worthwhile, doctors are conducting large studies to see if early detection tests will lower the risk of death from prostate cancer. The most recent results from 2 large studies were conflicting, and didn't offer clear answers.

Early results from a study done in the United States found that annual screening with PSA and DRE detected more prostate cancers than in men not screened, but it did not lower the death rate from prostate cancer. A European study did find a lower risk of death from prostate cancer with PSA screening (done about once every 4 years), but the researchers estimated that about 1,050 men would need to invited to be screened (and 37 treated) to prevent one death from prostate cancer. Neither of these studies has shown that PSA screening helps men live longer (lowered the overall death rate).

Prostate cancer is often a slow-growing cancer, so the effects of screening in these studies may become clearer in the coming years. Both of these studies are being continued to see

if longer follow-up will give clearer results. Several other large studies of prostate cancer screening are now going on as well.

At this time, the American Cancer Society (ACS) recommends that men thinking about prostate cancer screening should make informed decisions based on available information, discussion with their doctor, and their own views on the benefits and side effects of screening and treatment (see below).

Until more information is available, you and your doctor should decide whether you should have tests to screen for prostate cancer. There are many factors to take into account, including your age and health. If you are young and develop prostate cancer, it may shorten your life if it is not caught early. Screening men who are older or in poor health in order to find early prostate cancer is less likely to help them live longer. This is because most prostate cancers are slow-growing, and men who are older or sicker are likely to die from other causes before their prostate cancer grows enough to cause problems.

American Cancer Society recommendations for the early detection of prostate cancer

The American Cancer Society recommends that men have a chance to make an informed decision with their health care provider about whether to be screened for prostate cancer. The decision should be made after getting information about the uncertainties, risks, and potential benefits of prostate cancer screening. Men should not be screened unless they have received this information.

The discussion about screening should take place at age 50 for men who are at average risk of prostate cancer and are expected to live at least 10 more years.

This discussion should take place starting at age 45 for men at high risk of developing prostate cancer. This includes African-American men and men who have a first-degree relative (father, brother, or son) diagnosed with prostate cancer at an early age (younger than age 65).

This discussion should take place at age 40 for men at even higher risk (those with more than one first-degree relative who had prostate cancer at an early age).

After this discussion, those men who want to be screened should be tested with the prostate-specific antigen (PSA) blood test. The digital rectal exam (DRE) may also be done as a part of screening.

If, after this discussion, a man is unable to decide if testing is right for him, the screening decision can be made by the health care provider, who should take into account the patient’s general health preferences and values.

Assuming no prostate cancer is found as a result of screening, the time between future screenings depends on the results of the PSA blood test:

- Men who have a PSA less than 2.5 ng/ml may only need to be retested every 2 years.
- Screening should be done yearly for men whose PSA level is 2.5 ng/ml or higher.

Because prostate cancer often grows slowly, men without symptoms of prostate cancer who do not have a 10-year life expectancy should not be offered testing since they are not likely to benefit. Overall health status, and not age alone, is important when making decisions about screening.

Even after a decision about testing has been made, the discussion about the pros and cons of testing should be repeated as new information about the benefits and risks of testing becomes available. Further discussions are also needed to take into account changes in the patient's health, values, and preferences.

Prostate-specific antigen (PSA) blood test

Prostate-specific antigen (PSA) is a substance made by cells in the prostate gland (both normal cells and cancer cells). PSA is mostly found in semen, but a small amount is also found in the blood. Most healthy men have levels under 4 nanograms per milliliter (ng/mL) of blood. The chance of having prostate cancer goes up as the PSA level goes up.

When prostate cancer develops, the PSA level usually goes above 4. Still, a level below 4 does not guarantee that a man doesn't have cancer – about 15% of men with a PSA below 4 will have prostate cancer on biopsy. Men with a borderline PSA level between 4 and 10 have about a 1 in 4 chance of having prostate cancer. If the PSA is more than 10, the chance of having prostate cancer is more than 50%.

If your PSA level is high, your doctor may advise either waiting a while and repeating the test, or getting a prostate biopsy to find out if you have cancer (see the section “How is prostate cancer diagnosed?”). Not all doctors use the same PSA cutoff point when advising whether to do a biopsy. Some may advise it if the PSA is 4 or higher, while others might recommend it at 2.5 or higher. Other factors, such as your age, race, and family history, may also come into play.

Factors that might affect PSA levels

The PSA level can also be increased by things other than prostate cancer, such as:

- **An enlarged prostate:** Conditions such as *benign prostatic hyperplasia* (BPH), a non-cancerous enlargement of the prostate that affects many men as they grow older, may raise PSA levels.

- **Older age:** PSA levels normally go up slowly as you get older, even if you have no prostate abnormality.
- **Prostatitis:** This term refers to infection or inflammation of the prostate gland, which may raise PSA levels.
- **Ejaculation:** This can cause the PSA to go up for a short time, and then go down again. This is why some doctors suggest that men abstain from ejaculation for 2 days before testing.
- **Riding a bicycle:** Some studies have suggested that cycling may raise PSA levels (possibly because the seat puts pressure on the prostate), although not all studies have found this.
- **Certain urologic procedures:** Some procedures done in a doctor's office that affect the prostate, such as a prostate biopsy or cystoscopy, may result in higher PSA levels for a short time. Some studies have suggested that a digital rectal exam (DRE) might raise PSA levels slightly, although other studies have not found this. Still, if both a PSA test and a DRE are being done during a doctor visit, some doctors advise having the blood drawn for the PSA before having the DRE, just in case.
- **Certain medicines:** Taking male hormones like testosterone (or other medicines that raise testosterone levels) may cause a rise in PSA.

Some things may cause PSA levels to go down (even if cancer is present):

- **5-alpha reductase inhibitors:** Certain drugs used to treat BPH or urinary symptoms, such as finasteride (Proscar or Propecia) or dutasteride (Avodart), may lower PSA levels. These drugs can also affect prostate cancer risk (this was discussed in the section “Can prostate cancer be prevented?”). You should tell your doctor if you are taking these medicines, because they will lower PSA levels and require the doctor to adjust the reading.
- **Herbal mixtures:** Some mixtures that are sold as dietary supplements may also mask a high PSA level. This is why it is important to let your doctor know if you are taking any type of supplement, even ones that are not necessarily meant for prostate health. Saw palmetto (an herb used by some men to treat BPH) does not seem to affect PSA.
- **Obesity:** Obese men tend to have lower PSA levels.
- **Aspirin:** Some recent research has suggested that men who take aspirin regularly may have lower PSA levels. This effect may be greater in non-smokers. More research is needed to confirm this finding. If you take aspirin regularly (such as to help prevent heart disease), talk to your doctor before you stop taking it for any reason.

- **Statins:** Cholesterol-lowering drugs known as statins, such as atorvastatin (Lipitor®), rosuvastatin (Crestor®), and simvastatin (Zocor®), are linked to lower PSA levels if taken over years. However, this effect on PSA levels is not seen if calcium channel blockers are taken at the same time. Calcium channel blockers, such as diltiazem (Cardizem®), amlodipine (Norvasc®), and verapamil (Calan®), are drugs used to treat high blood pressure and heart problems.
- **Thiazide diuretics:** Thiazide diuretics, such as hydrochlorothiazide (HCTZ), are a type of water pill often used to treat high blood pressure. Taking a thiazide diuretic for years is linked to lower PSA levels. Taking both a thiazide diuretic and a statin is linked to even lower PSA levels than with either type of drug alone.

For men not known to have prostate cancer, it is not always clear if lowering the PSA is helpful. In some cases the factor that lowers the PSA may also lower a man's risk of prostate cancer. But in other cases, it might lower the PSA level without affecting a man's risk of cancer. This could actually be harmful, if it were to lower the PSA from an abnormal level to a normal one, as it might result in not detecting a cancer. This is why it is important to talk to your doctor about anything that might affect your PSA level.

Special types of PSA tests

Some doctors might consider using special types of PSA tests 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 (between 4 and 10). 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 and helps some men avoid unnecessary prostate biopsies. This test is widely used, but not all doctors agree that 25% is the best cutoff point to decide on a biopsy, and the cutoff may change depending on PSA level.

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. Normally, PSA levels go up slowly with age. Some research has found that these levels go up faster if a man has cancer, but studies have not shown that the PSA velocity is more helpful than the PSA level itself in finding prostate cancer. For this reason, the ACS guideline does not recommend using the PSA velocity as part of screening for prostate cancer.

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 in "How is prostate cancer diagnosed?") and divides the PSA number by the prostate volume. A higher PSA density (PSAD) indicates a greater likelihood of cancer. PSA density has not been shown to be as useful as the percent-free PSA test.

Age-specific PSA ranges

PSA levels are normally higher in older men than in younger men, even when there is no cancer. 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. 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.

Other uses of the PSA blood test

The PSA test is used mainly to detect prostate cancer early, but it is also useful if prostate cancer has been diagnosed. For more information on the other uses of PSA testing, see the sections "How is prostate cancer diagnosed?" and "Following PSA levels during and after treatment."

Digital rectal exam (DRE)

For a digital rectal exam (DRE), a doctor inserts a gloved, lubricated finger into the rectum to feel for any bumps or hard areas on the prostate that might be cancer. The prostate gland is 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. This exam can be uncomfortable (especially in men who have hemorrhoids), but it usually isn't painful and only takes a short time.

DRE is less effective than the PSA blood test in finding prostate cancer, but it can sometimes find cancers in men with normal PSA levels. For this reason, it may be included as a part of prostate cancer screening.

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

Signs and symptoms of prostate cancer

Early prostate cancer usually causes no symptoms. Advanced prostate cancers can cause some symptoms, such as:

- Problems passing urine, including a slow or weak urinary stream or the need to urinate more often, especially at night.
- Blood in the urine (*hematuria*)
- Trouble getting an erection (*impotence*)
- Pain in the hips, back (spine), chest (ribs), or other areas from cancer spread to bones
- Weakness or numbness in the legs or feet, or even loss of bladder or bowel control from cancer pressing on the spinal cord.

Other diseases can also cause many of these same symptoms. For example, trouble passing urine is much more often caused by benign prostatic hyperplasia (BPH) than cancer. Still, it is important to tell your doctor if you have any of these problems so that the cause can be found and treated, if needed.

How is prostate cancer diagnosed?

Most prostate cancers are first found during screening with a prostate-specific antigen (PSA) blood test and or a digital rectal exam (DRE). (See "Can prostate cancer be found early?") Early prostate cancers usually do not cause symptoms, but more advanced cancers are sometimes first found because of symptoms they cause. Whether cancer is suspected based on screening tests or symptoms, the actual diagnosis can only be made with a prostate biopsy.

Medical history and physical exam

If your doctor suspects you might have prostate cancer, he or she will ask you about any symptoms you are having, such as any urinary or sexual problems, and how long you

have had them. Your doctor may also ask about bone pain, which could be a sign that the cancer might have spread to your bones.

Your doctor will also physically examine you, including doing a digital rectal exam (DRE), during which a gloved, lubricated finger is inserted into the rectum to feel for any bumps or hard areas on the prostate that might be cancer.

If you do have cancer, the DRE can sometimes help tell if it is only on one side of the prostate, if it is on both sides, or if it is likely to have spread beyond the prostate to nearby tissues.

Your doctor may also examine other areas of your body to see if the cancer has spread. He or she will then order some tests.

PSA blood test

The prostate-specific antigen (PSA) blood test is used mainly to try to find prostate cancer early in men without symptoms (see "Can prostate cancer be found early?"). But it is also one of the first tests done in men who have symptoms that might be caused by prostate cancer.

The PSA test can also be useful if prostate cancer has already been diagnosed.

- In men just diagnosed with prostate cancer, the PSA test can be used together with physical exam results and tumor grade (from the biopsy, described further on) to help decide if other tests (such as CT scans or bone scans) are needed.
- The PSA test is a part of staging and can help tell if your cancer is likely to be still confined to the prostate gland. If your PSA level is very high, your cancer has probably 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.

PSA tests are also an important part of monitoring prostate cancer during and after treatment (see "Following PSA levels during and 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 that gives off sound waves is placed into the rectum. The sound waves 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 often takes less than 10 minutes and is done in a doctor's office or outpatient clinic. The ultrasound probe is about the width of a finger and is lubricated

before it is placed in your rectum. You will feel some pressure when the probe is inserted, but it is usually not painful. The area may be numbed before the procedure.

TRUS is often used to look at the prostate when a man has a high PSA level or has an abnormal DRE. It is also used during a prostate biopsy to guide the 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 (described in "Can prostate cancer be found early?") and may also affect which treatment options a man has. TRUS is also used as a guide during some forms of treatment such as brachytherapy (internal radiation therapy) or cryosurgery.

Prostate biopsy

If certain symptoms or the results of early detection tests – a PSA blood test and/or DRE – suggest that you might have prostate cancer, your doctor will do a prostate biopsy to find out.

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 to "see" the prostate gland, the doctor quickly inserts a thin, hollow needle through the wall of the rectum into the prostate gland. When the needle is pulled out it removes a small cylinder (core) of prostate tissue. This is repeated from 8 to18 times, but most urologists will take about 12 samples.

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

The biopsy itself takes about 10 minutes and is usually done in the doctor's office. You will likely be given antibiotics to take before the biopsy and possibly 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 probably notice blood in your urine. You may also have some light bleeding from your rectum, especially if you have hemorrhoids. Many men also see some blood in their semen or have rust colored semen, which can last for several weeks after the biopsy, depending on how frequently you ejaculate.

Your biopsy samples will be sent to a lab, where a *pathologist* (a doctor who specializes in diagnosing disease in tissue samples) will look at them under a microscope to see if they contain cancer cells. If cancer is present, the pathologist will also assign it a *grade* (see the next section). Getting the results usually takes at least 1 to 3 days, but it can take longer.

Even taking 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 you have prostate cancer (due to a very high PSA level, for example) a repeat biopsy may be needed to help be sure.

Grading prostate cancer

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 cells and their growth patterns look very abnormal, it is called a *grade 5* tumor.
- Grades 2 through 4 have features in between these extremes.

Today, most biopsies are grade 3 or higher, and grades 1 and 2 are not often used.

Since 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). The Gleason score can be between 2 and 10, but most biopsies are at least a 6.

There are some exceptions to this rule. If the highest grade takes up most (95% or more) of the biopsy, the grade for that area is counted twice as the Gleason score. Also, if 3 grades are present in a biopsy core, the highest grade is always included in the Gleason score, even if most of the core is taken up by areas of cancer with lower grades.

- Cancers with a Gleason score of 6 or less are often called *well-differentiated* or *low-grade*.
- Cancers with a Gleason score of 7 may be called *moderately differentiated* or *intermediate-grade*.
- Cancers with Gleason scores of 8 to 10 may be called *poorly differentiated* or *high-grade*.

The higher the Gleason score, the more likely it is that your cancer will grow and spread quickly.

Other information in a biopsy report

Along with the grade of the cancer (if it is present), the pathologist's report also 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) of the prostate or both sides (bilateral)

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*.

Prostatic intraepithelial neoplasia (PIN): In PIN, there are changes in how the prostate cells look under the microscope, but the abnormal cells don't look like they've grown 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 but do not necessarily develop prostate cancer. The importance of low-grade PIN in relation to prostate cancer is still unclear. If a finding of low-grade PIN is reported on a prostate biopsy, the follow-up for patients is usually the same as if nothing abnormal was seen.

If high-grade PIN is found on a biopsy, there is about a 20% to 30% chance that cancer may already be present somewhere else in the prostate gland. This is why 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.

Atypical small acinar proliferation (ASAP): This 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 a high chance that cancer is also present in the prostate, which is why many doctors recommend getting a repeat biopsy within a few months.

Proliferative inflammatory atrophy (PIA): In PIA, the prostate cells look smaller than normal, and there are signs of inflammation in the area. PIA is not cancer, but researchers believe that PIA may sometimes lead to high-grade PIN or to prostate cancer directly.

For more information about how biopsy results are reported, see the “Prostate Pathology” section of our website.

Imaging tests to look for prostate cancer spread

If you are found to have prostate cancer, 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 the cancer has spread outside your prostate. This information is used to decide if any imaging tests need to be done to look for possible cancer spread in the body. Imaging tests use x-rays, magnetic fields, sound waves, or radioactive substances to create pictures of the inside of your body.

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.

The imaging tests used most often to look for prostate cancer spread include:

Bone scan

If prostate cancer spreads to distant sites, it often goes to the bones first. (Even when prostate cancer spreads to the bone, it is still 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 areas of bone throughout the body 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. Hot spots may suggest cancer in the bone, but arthritis or other bone diseases can also cause hot spots. To make an accurate diagnosis, other imaging tests such as plain x-rays, CT or MRI scans, or even a bone biopsy might be needed.

The injection 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. The amount of radioactivity used is very low, so it carries very little risk to you or others. But you still might want to ask your doctor if you should take any special precautions after having this test.

Computed tomography (CT)

This test can sometimes help tell if prostate cancer has spread into nearby lymph nodes. Still, for newly diagnosed prostate cancers it isn’t often needed if the cancer is likely to be confined to the prostate based on other findings (DRE result, PSA level, and Gleason

score). 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.

The CT scan (also known as a *CAT scan*) is a special kind of x-ray test 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 as it rotates around you. A computer then combines these pictures into images of slices of the part of your body being studied. Unlike a regular x-ray, a CT scan creates detailed images of the soft tissues in the body.

For some scans, you may be asked to drink 1 or 2 pints of oral contrast before the first set of pictures is taken. This helps outline the intestine so that it looks different from any tumors. You may receive an IV (intravenous) line through which a different kind of contrast is injected. This helps better outline structures in your body.

The IV contrast can cause your body to feel flushed (a feeling of warmth with some redness of the skin). A few people are allergic and get hives. Rarely, more serious reactions, like trouble breathing or low blood pressure, can occur. Medicines can be given to prevent and treat allergic reactions, so be sure to tell your doctor if you have any allergies or have ever had a reaction to any contrast material used for x-rays.

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.

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 slides in and out of the scanner, a ring-shaped machine that surrounds the table. You might feel a bit confined by the ring while the pictures are being taken.

CT scans are not as useful as magnetic resonance imaging (MRI) for looking at the prostate gland itself.

Magnetic resonance imaging (MRI)

MRI scans can be 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 other nearby structures. This information can be very important for your doctors in planning your treatment. But like CT scans, MRI scans may not provide useful information about newly diagnosed prostate cancers that are likely to be confined to the prostate based on other factors.

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. Like a CT scan, a contrast material might be injected, but this is done less often. Because the scanners use magnets, people with pacemakers, certain heart valves, or other medical implants may not be able to get an MRI.

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 noise 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. If needed, medicine to make you feel sleepy (sedation) can be given before the scan.

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 contains 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.

This test can find prostate cancer cells in lymph nodes and other soft (non-bone) organs, although it is not as helpful for looking at the area around the prostate itself. The antibody only sticks to prostate cells, so other cancers or benign problems should not cause abnormal results. 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 after treatment if your blood PSA level begins to rise 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

In a lymph node biopsy, also known as *lymph node dissection* or *lymphadenectomy*, one or more lymph nodes are removed to see if they contain cancer cells. This isn’t done very often for prostate cancer, but can be done to find out whether the cancer has spread from the prostate to nearby lymph nodes. 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 "Surgery for prostate cancer" for information about radical prostatectomy.)

If there is more than a very small chance that the cancer might have spread (based on factors such as a high PSA level or a high Gleason score), the surgeon may remove some lymph nodes before attempting to remove the prostate gland.

In some cases a pathologist will look at the nodes right away, 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 might be stopped (leaving the prostate in place). This would happen if the surgeon felt that removing the prostate would be unlikely to cure the cancer, but would still probably result in serious complications or side effects.

But more often (especially if the chance of cancer spread is low), a frozen section exam is not done. Instead the lymph nodes and the prostate are removed and are then sent to the lab to be looked at. The lab results are usually available several days after surgery.

Laparoscopic biopsy

A laparoscope is a long, slender tube with a small video camera on the end that is inserted into the abdomen through a cut about the size of the width of a finger. It lets the surgeon see inside the abdomen and pelvis without needing to make a large incision. Other small incisions are made to insert long instruments to remove the lymph nodes. The surgeon then removes 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 if the lymph nodes contain cancer but a 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 test (such as a CT or MRI scan) a specially trained radiologist may take a sample of cells from an enlarged node by using a technique called fine needle aspiration (FNA).

To do this, the doctor uses a CT scan image to guide a long, thin needle through the skin in the lower abdomen and into the enlarged node. Before the needle is placed, your skin

will be numbed with local anesthesia. A syringe attached to the needle lets the doctor take a small tissue sample from the node, which is then sent to a pathologist to look for cancer cells.

You will be able to return home a few hours after the procedure.

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 man's outlook. The stage is based on the prostate biopsy results (including the Gleason score), the PSA level, and any other exams or tests that were done to find out how far the cancer has spread. These tests are described in the section "How is prostate cancer diagnosed?"

The AJCC TNM staging system

A staging system is a standard way for the cancer care team to describe how far a cancer has spread. The most widely used staging system for prostate cancer is the American Joint Committee on Cancer (AJCC) TNM system.

The TNM system for prostate cancer is based on 5 key pieces of information:

- 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 PSA level at the time of diagnosis
- The Gleason score, based on the prostate biopsy (or surgery)

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 tests 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 active surveillance.

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

T categories (clinical)

There are 4 categories for describing the local extent of a 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:** Cancer is found incidentally (by accident) during a transurethral resection of the prostate (TURP) that was done for benign prostatic hyperplasia (BPH). Cancer is in no more than 5% of the tissue removed.
- **T1b:** Cancer is found during a TURP but is in more than 5% of the tissue removed.
- **T1c:** Cancer is found by needle biopsy that was done because of an increased PSA.

T2: Your doctor can feel the cancer with a digital rectal exam (DRE) or see it with imaging such as transrectal ultrasound, 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 grow and spread outside your prostate and may have spread into 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 grown into tissues next to your prostate (other than the seminal vesicles), such as the urethral sphincter (muscle that helps control urination), the rectum, the bladder, and/or the wall of the pelvis.

N categories

N categories describe whether the cancer has spread to nearby (regional) lymph nodes.

NX: Nearby lymph nodes were not assessed.

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

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

M categories

M categories describe whether the cancer has spread to distant parts of the body. The most common sites of prostate cancer spread are to the bones and to distant lymph nodes, although it can also spread to other organs, such as the lungs and liver.

M0: The cancer has not spread past nearby lymph nodes.

M1: The cancer has spread beyond the nearby lymph 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 spread to the bones).

Stage grouping

Once the T, N, and M categories have been determined, this information is combined, along with the Gleason score and prostate-specific antigen (PSA), in a process called *stage grouping*. If the Gleason score or PSA results are not available, the stage can be based on the T, N, and M categories. 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 (prognosis).

Stage I: One of the following applies:

T1, N0, M0, Gleason score 6 or less, PSA less than 10: The doctor can't feel the tumor or see it with an imaging test such as transrectal ultrasound (it was either found during a transurethral resection or was diagnosed by needle biopsy done for a high PSA) [T1]. The cancer is still within the prostate and has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Gleason score is 6 or less and the PSA level is less than 10.

OR

T2a, N0, M0, Gleason score 6 or less, PSA less than 10: The tumor can be felt by digital rectal exam or seen with imaging such as transrectal ultrasound and is in one half or less of only one side (left or right) of your prostate [T2a]. The cancer is still within the prostate and has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Gleason score is 6 or less and the PSA level is less than 10.

Stage IIA: One of the following applies:

T1, N0, M0, Gleason score of 7, PSA less than 20: The doctor can't feel the tumor or see it with imaging such as transrectal ultrasound (it was either found during a

transurethral resection or was diagnosed by needle biopsy done for a high PSA level) [T1]. The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The tumor has a Gleason score of 7. The PSA level is less than 20.

OR

T1, N0, M0, Gleason score of 6 or less, PSA at least 10 but less than 20: The doctor can't feel the tumor or see it with imaging such as transrectal ultrasound (it was either found during a transurethral resection or was diagnosed by needle biopsy done for a high PSA) [T1]. The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The tumor has a Gleason score of 6 or less. The PSA level is at least 10 but less than 20.

OR

T2a or T2b, N0, M0, Gleason score of 7 or less, PSA less than 20: The tumor can be felt by digital rectal exam or seen with imaging such as transrectal ultrasound and is in only one side of the prostate [T2a or T2b]. The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. It has a Gleason score of 7 or less. The PSA level is less than 20.

Stage IIB: One of the following applies:

T2c, N0, M0, any Gleason score, any PSA: The tumor can be felt by digital rectal exam or seen with imaging such as transrectal ultrasound and is in both sides of the prostate [T2c]. The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The tumor can have any Gleason score and the PSA can be any value.

OR

T1 or T2, N0, M0, any Gleason score, PSA of 20 or more: The cancer has not yet begun to spread outside the prostate. It may (or may not) be felt by digital rectal exam or seen with imaging such as transrectal ultrasound [T1 or T2]. The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The tumor can have any Gleason score. The PSA level is at least 20.

OR

T1 or T2, N0, M0, Gleason score of 8 or higher, any PSA: The cancer has not yet begun to spread outside the prostate. It may (or may not) be felt by digital rectal exam or seen with imaging such as transrectal ultrasound [T1 or T2]. The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The Gleason score is 8 or higher. The PSA can be any value.

Stage III:

T3, N0, M0, any Gleason score, any PSA: The cancer has begun to spread outside the prostate and may have spread to the seminal vesicles [T3], but it has not spread to nearby

lymph nodes [N0] or elsewhere in the body [M0]. The tumor can have any Gleason score and the PSA can be any value.

Stage IV: One of the following applies:

T4, N0, M0, any Gleason score, any PSA: The cancer has spread to tissues next to the prostate (other than the seminal vesicles), such as the urethral sphincter (muscle that helps control urination), rectum, bladder, and/or the wall of the pelvis [T4]. The cancer has not spread to nearby lymph nodes [N0] or elsewhere in the body [M0]. The tumor can have any Gleason score and the PSA can be any value.

OR

Any T, N1, M0, any Gleason score, any PSA: The tumor may or may not be growing into tissues near the prostate [any T]. The cancer has spread to nearby lymph nodes (N1) but has not spread elsewhere in the body [M0]. The tumor can have any Gleason score and the PSA can be any value.

OR

Any T, any N, M1, any Gleason score, any PSA: The cancer may or may not be growing into tissues near the prostate [any T] and may or may not have spread to nearby lymph nodes [any N]. It has spread to other, more distant sites in the body [M1]. The tumor can have any Gleason score and the PSA can be any value.

Other staging systems

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 the Whitmore-Jewett system, ask them to translate it into the TNM system or to explain how their staging will determine your treatment options.

The D’Amico risk categories

The D’Amico system is not used to stage all cases of prostate cancer like the AJCC system. It is sometimes used to look at the risk that a prostate cancer has spread outside the prostate. This system uses the man’s PSA level, the Gleason score of the cancer, and the T stage of the cancer to divide men into 3 risk groups: low, intermediate, and high.

Survival rates for prostate cancer

Survival rates are often used by doctors as a standard way of discussing a person's prognosis (outlook). Some patients with cancer may want to know the survival statistics for people in similar situations, while others may not find the numbers helpful, or may

even not want to know them. If you would rather not read the survival rates, skip to the next section.

The 5-year survival rate refers to the percentage of patients who live *at least 5 years* after their cancer is diagnosed. Of course, many of these people live much longer than 5 years (and many are cured).

Five-year *relative* survival rates, such as the numbers below, assume that some people will die of other causes and compare the observed survival with that expected for people without the cancer. This is a better way to see the impact of the cancer on survival.

In order to get 5-year survival rates, doctors have to look at people who were treated at least 5 years ago. Improvements in detection and treatment since then may result in a more favorable outlook for people now being diagnosed with prostate cancer.

Survival rates are often based on previous outcomes of large numbers of people who had the disease, but they cannot predict what will happen in any particular person's case. Many other factors may affect a person's outlook, such as the patient’s age and health, the treatment received, and how well the cancer responds to treatment. Your doctor can tell you how the numbers below may apply to you, as he or she is familiar with the aspects of your particular situation.

According to the most recent data, when including *all* stages of prostate cancer:

- The relative 5-year survival rate is almost 100%
- The relative 10-year survival rate is 99%
- The 15-year relative survival rate is 94%

Keep in mind that just as 5-year survival rates are based on patients diagnosed and first treated more than 5 years ago,10-year survival rates are based on patients diagnosed more than 10 years ago (and 15-year survival rates are based on patients diagnosed at least 15years ago).

Survival rates by stage

The National Cancer Institute (NCI) maintains a large national database on survival statistics for different types of cancer. This database does not group cancers by AJCC stage, but instead groups cancers into local, regional, and distant stages.

- **Local stage** means that there is no sign that the cancer has spread outside of the prostate. This corresponds to AJCC stages I and II. About 4 out of 5 prostate cancers are found in this early stage.
- **Regional stage** means the cancer has spread from the prostate to nearby areas. This includes stage III cancers and the stage IV cancers that haven't spread to distant parts

of the body, such as T4 tumors and cancers that have spread to nearby lymph nodes (N1).

- **Distant stage** includes the rest of the stage IV cancers – all cancers that have spread to distant lymph nodes, bones, or other organs (M1).

5-year relative survival by stage at the time of diagnosis

Stage	**5-year relative survival rate**
local	nearly 100%
regional	nearly 100%
distant	28%

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.

Some general comments about prostate cancer treatment

Once your prostate cancer has been diagnosed 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?"

Depending on the situation, the treatment options for men with prostate cancer may include:

- Expectant management (watchful waiting) or active surveillance
- Surgery
- Radiation therapy
- Cryosurgery (cryotherapy)
- Hormone therapy
- Chemotherapy
- Vaccine treatment
- Bone directed treatment

These treatments are generally used one at a time, although in some cases they may be combined.

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 possible side effects from each treatment

Many men find it helpful to get a second opinion about the best treatment options based on their situation, especially if there are several choices available. 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 help you sort through your options. You will want to weigh the benefits of each treatment against its possible outcomes, side effects, and risks.

The main types of doctors who treat prostate cancer include:

- Urologists: surgeons who specialize in treating diseases of the urinary system and male reproductive system (including the prostate)
- Radiation oncologists: doctors who treat cancer with radiation therapy

- Medical oncologists: doctors who treat cancer with medicines such as chemotherapy or hormone therapy

It is important to discuss all of your treatment options, including goals and possible side effects, with your doctors to help make the decision that best fits your needs.

Once you decide on a treatment plan, many other specialists may be involved in your care as well, including nurse practitioners, nurses, nutrition specialists, social workers, and other health professionals. If you'd like to know more about who may be on your cancer care team, see our document *Health Professionals Associated With Cancer Care.*

The next few sections describe the types of treatments used for prostate cancer. This is followed by discussion of other treatment-related topics, including things to think about when considering treatment options, typical treatment options based on the stage of the cancer, following PSA levels during and after treatment, and dealing with prostate cancer that remains or recurs after treatment.

Expectant management (watchful waiting) and active surveillance for prostate cancer

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 approaches known as *expectant management*, *watchful waiting*, or *active surveillance*.

Some doctors use these terms to mean the same thing. For other doctors the terms active surveillance and watchful waiting mean something slightly different:

Active surveillance is often used to mean monitoring the cancer closely with prostate-specific antigen (PSA) blood tests, digital rectal exams (DREs), and ultrasounds at regular intervals to see if the cancer is growing. Prostate biopsies may be done as well to see if the cancer is becoming more aggressive. If there is a change in your test results, your doctor would then talk to you about treatment options.

Watchful waiting is sometimes used to describe a less intensive type of follow-up that may mean fewer tests and relying more on changes in a man's symptoms to decide if treatment is needed.

Not all doctors agree with these definitions or use them exactly this way. In fact, some doctors prefer to no longer use the term watchful waiting. They feel it implies that nothing is being done, when in fact a man is still being closely monitored. **No matter which term your doctor may use, it is very important to understand exactly what he or she means when they refer to it.**

With active surveillance, your cancer will be carefully monitored. Usually this approach includes a doctor visit with a PSA blood test and DRE about every 3 to 6 months. Transrectal ultrasound-guided prostate biopsies may be done every year as well.

Treatment can be started if the cancer seems to be growing or getting worse, based on a rising PSA level or a change in the DRE, ultrasound findings, or biopsy results. On biopsies, an increase in the Gleason score or extent of tumor (based on the number of biopsy samples containing tumor) are both signals to start treatment (usually surgery or radiation therapy).

Active surveillance allows the patient to be observed for a time, only treating those men whose cancer grows, and so have a serious form of the cancer. This lets men with a less serious cancer avoid the side effects of a treatment that might not have helped them live longer. A possible downside of this approach is that there's a chance it could allow the cancer to spread. This could limit your treatment options, and could possibly affect the chance to cure the cancer.

An approach such as this may be recommended if your cancer is not causing any symptoms, is expected to grow slowly (based on Gleason score), and is small and contained within the prostate. This type of approach is not likely to be a good option if you have a fast-growing cancer (for example, a high Gleason score) or if the cancer is likely to have spread outside the prostate (based on PSA levels). Men who are young and healthy are less likely to be offered active surveillance, out of concern that the cancer will become a problem over the next 20 or 30 years.

Active surveillance is a reasonable option for some men with slow-growing cancers because it is not known whether treating the cancer with surgery or radiation will actually help them live longer. These treatments have definite risks and side effects that may outweigh the possible benefits for some men. Some men 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.

Not all experts agree how often testing should be done during active surveillance. There is also debate about when is the best time to start treatment if things change.

There have been a few randomized studies comparing watchful waiting (where men were only treated if they developed symptoms from their cancer) and surgery for early stage prostate cancer. In one study, where few of the patients had very early (T1) cancers, the men who had surgery lived longer. In the other, where about half of the men had very early cancers, there was no real survival advantage for treatment with surgery.

So far there are no randomized studies comparing active surveillance to treatments such as surgery or radiation therapy. Some early studies of active surveillance (in men who are good candidates) have shown that only about a quarter of the men need to go on to definitive treatment with radiation or surgery.

Surgery for prostate cancer

Surgery is a common choice to try to cure prostate cancer if it is not thought to have spread outside the gland (stage T1 or T2 cancers).

The main type of surgery for prostate cancer is known as a *radical prostatectomy*. In this operation, the surgeon removes the entire prostate gland plus some of the tissue around it, including the seminal vesicles. A radical prostatectomy can be done in different ways.

Open approaches to radical prostatectomy

In the more traditional approach to doing a prostatectomy, the surgeon operates through a single long incision to remove the prostate and nearby tissues. This is sometimes referred to as an *open* approach.

Radical retropubic prostatectomy

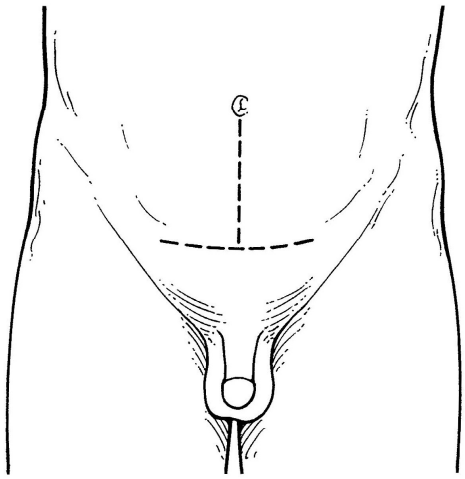
For this operation, the surgeon makes a skin incision in your lower abdomen, from the belly button down to the pubic bone. You will be either under general anesthesia (asleep) or be given spinal or epidural anesthesia (numbing the lower half of the body) along with sedation during the surgery.

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. The nodes are usually sent to the pathology lab to see if they have cancer cells (it takes a few days to get results), but in some cases the nodes may be looked at right away. If this is done during surgery and any of the nodes have cancer cells, which means the cancer has spread, the surgeon may not continue with the surgery. This is because it is unlikely that the cancer can be cured with surgery, and removing the prostate could still lead to serious side effects.

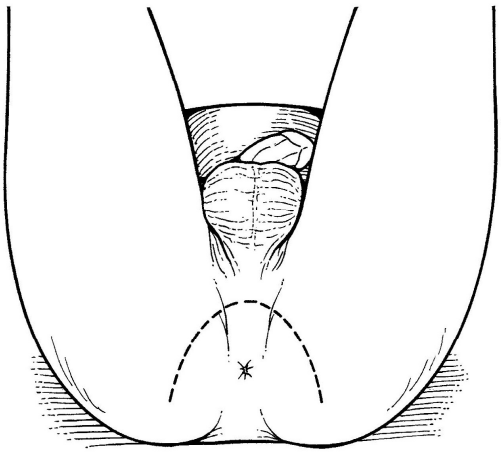
When removing the prostate, the surgeon will pay close attention to the 2 tiny bundles of nerves that run on either side of the prostate. These nerves control erections. If you are able to have erections before surgery, the surgeon will try not to injure these nerves (known as a *nerve-sparing* approach). 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 unable to have spontaneous erections. This means that you will need help (such as medicines or pumps) to have erections. If the nerves on one side are removed, you still have a chance of keeping your ability to have erections, but the chance 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 to a year after surgery to have an erection because the nerves have been handled during the operation and won't work properly for a while.

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 2 weeks while you are healing. You will be able to urinate on your own after the catheter is removed.

You will probably stay in the hospital for a few days after the surgery and be limited in your activities for about 3 to 5 weeks. The possible side effects of prostatectomy are described below.



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 and you don't 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 approach if done correctly. The perineal operation usually takes less time than the retropubic operation, and may result in less pain and an easier recovery afterward.

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 2 weeks while you are healing. You will be able to urinate on your own after the catheter is removed.

You will probably stay in the hospital for a few days after the surgery and be limited in your activities for about 3 to 5 weeks. The possible side effects of prostatectomy are described below.

Laparoscopic approaches to radical prostatectomy

Laparoscopic approaches use several smaller incisions and special surgical tools to remove the prostate. This can be done with the surgeon either holding the tools directly, or using a control panel to precisely move robotic arms that hold the tools.

Laparoscopic radical prostatectomy

For a laparoscopic radical prostatectomy (LRP), the surgeon makes several small 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 lets the surgeon 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 has been used in the United States since 1999 and is 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. (These side effects are described below.) Recovery of bladder control may be slightly delayed with this approach. A nerve-sparing approach is possible with LRP, increasing the chance of normal erections after the operation.

Robotic-assisted laparoscopic radical prostatectomy

A newer approach is to do the laparoscopic surgery remotely using a robotic interface (called the da Vinci system), which is known as *robotic-assisted laparoscopic radical prostatectomy* (RALRP). 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.

Like direct LRP, RALRP has advantages over the open approach in terms of pain, blood loss, and recovery time. So far though, there seems to be little difference between robotic and direct LRP for the patient.

In terms of the side effects men are most concerned about, such as urinary problems or erectile dysfunction (described below), there does not seem to be a difference between robotic-assisted LRP and other approaches to prostatectomy.

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

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 either type of LRP is the treatment for you, be sure to find a surgeon with a lot of experience.

Possible risks and 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 with 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.

If lymph nodes are removed, a collection of lymph fluid (called a *lymphocele*) can form and may need to be drained.

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. Rarely, part of the intestine might be cut during surgery, which could lead to infections in the abdomen and might require more surgery to correct. Injuries to the intestines are more common with laparoscopic and robotic surgeries than with the open approach.

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.

Side effects

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 can also occur with other forms of treatment for prostate cancer, although they are described here in more detail.

Urinary incontinence: You may develop urinary incontinence, which means you are not able to 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 major types of incontinence:

- **Stress incontinence** is the most common type of incontinence after prostate surgery. 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.

- Men with **overflow incontinence** cannot empty the bladder well. They 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 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 it fills with urine.

Rarely after surgery, men lose all ability to control their urine. This is called *continuous incontinence*.

After surgery for prostate cancer, normal bladder control usually returns within several weeks or months. This recovery usually occurs gradually, in stages.

Doctors can't predict for sure how any man will be affected after surgery. In general older men tend to have more incontinence problems than younger men.

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

Incontinence can be treated. Even if your incontinence cannot completely be corrected, it can still be helped. You can learn how to manage and live with incontinence. See our document called *Managing Incontinence for Men With Cancer* to learn more about this side effect and what can be done about it.

Impotence (erectile dysfunction): This 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 (besides surgery) may also damage these nerves or the blood vessels that supply blood to the penis to cause an erection.

Your ability to have an erection after surgery depends on your age, your ability to get an erection before the operation, and whether the nerves were cut. Everyone can expect some decrease in the ability to have an erection, but the younger you are, the more likely it is that you will keep this ability.

A wide range of impotency rates have been reported in the medical literature, from as low as about 1 in 4 men under age 60 to as high as about 3 in 4 men over age 70. Doctors who perform many nerve-sparing radical prostatectomies tend to report lower impotence rates than doctors who do the surgery less often.

Each man's situation is different, so the best way to get an idea of your chances for recovering erections is to ask your doctor about his or her success rates and what the outcome is likely to be in your particular case.

If your ability to have erections does return after surgery, it often occurs slowly. In fact, it can take up to 2 years. 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.

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 several weeks after the operation). Some doctors call this *penile rehabilitation*. 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 that control erections 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. Rarely, these drugs can cause vision problems, possibly even blindness. 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.

- *Alprostadil* is a man-made version of prostaglandin E1, a substance naturally made in the body that can produce erections. It can be injected almost painlessly into the base of the penis 5 to 10 minutes before intercourse or placed 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 to produce an erection. The erection is maintained after the pump is removed by a strong rubber band placed at the base of the penis. The band is removed by cutting it off when intercourse is done.

- *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 for the Man With Cancer*.

Changes in orgasm: In some men, orgasm becomes less intense or goes away completely. A few men report pain with orgasm. Even if you have problems with impotence, you may still be able to have an orgasm.

Loss of fertility: Radical prostatectomy cuts the connection between the testicles (where sperm are produced) and the urethra. Your testicles will still produce sperm, but it can't get out as a part of the ejaculate. 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 might want to ask 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 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 go away completely.

Change in penis length: A possible effect of surgery is a small decrease in penis length. This is probably due to a shortening of the urethra when a portion of it is removed along with the prostate.

Inguinal hernia: A prostatectomy increases a man's chances of developing an inguinal (groin) hernia in the future.

Transurethral resection of the prostate (TURP)

This operation is more commonly used to treat men with non-cancerous enlargement of the prostate called *benign prostatic hyperplasia* (BPH). A TURP is not used to try to cure prostate cancer, but it is sometimes used in men with advanced prostate cancer to help relieve symptoms, such as urination problems.

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, either electricity is passed through a wire to heat it or a laser is used to cut or vaporize the tissue. 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 about a day to help urine drain while the

prostate heals. You can usually leave the hospital after 1 to 2 days and return to normal activities in 1 to 2 weeks.

You will probably have some blood in your urine after surgery. Other possible side effects from TURP include infection and any risks that come with the type of anesthesia that was used.

Radiation therapy for prostate cancer

Radiation therapy uses high-energy rays or particles to kill cancer cells. Radiation may be used:

- As the initial treatment for low-grade cancer that is still confined within the prostate gland. Cure rates for men with these types of cancers are about the same as those for men getting radical prostatectomy.
- As part of the first treatment (along with hormone therapy) for cancers that have grown outside of the prostate gland and into nearby tissues.
- If the cancer is not completely removed or comes back (recurs) in the area of the prostate after surgery.
- If the cancer is advanced, to reduce the size of the tumor and to provide relief from present and possible future symptoms.

Two main types of radiation therapy can be 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. (Another type of radiation therapy, in which a medicine containing radiation is injected into the body, is described in the section "Preventing and treating prostate cancer spread to the bone.")

External beam radiation therapy (EBRT)

In EBRT, beams of radiation are focused on the prostate gland from a machine outside the body. This type of radiation can be used to try to cure earlier stage cancers, or to help relieve symptoms such as bone pain if the cancer has spread to a specific area of bone.

To reduce the risk of side effects, doctors carefully figure out the exact dose of radiation needed and aim the beams as accurately as they can to hit the carefully outlined target. Before treatments start, imaging tests 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 a week in an outpatient center for 7 to 9 weeks. Each treatment is much like getting an x-ray. The radiation is stronger than that used for an x-ray, but the procedure is painless. Each treatment lasts only a few minutes, although the setup time — getting you into place for treatment — takes longer.

EBRT for prostate cancer is most often given using techniques that let doctors give higher doses of radiation to the prostate gland while reducing the radiation exposure to nearby healthy tissues.

Three-dimensional conformal radiation therapy (3D-CRT)

3D-CRT uses special computers to precisely map the location of your prostate. Radiation beams are then shaped and aimed at the prostate from several directions, which makes it less likely to damage normal tissues. You will most likely be fitted with a plastic mold resembling a body cast to keep you in the same position each day so that the radiation can be aimed more accurately. This method seems to be at least as effective as standard radiation therapy with lower side effects.

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 lets doctors deliver an even higher dose to the cancer areas. This is the most common method of giving external beam radiation for prostate cancer.

Some newer radiation machines have imaging scanners built into them. This advance, known as *image guided radiation therapy* (IGRT), lets the doctor take pictures of the prostate and make minor adjustments in aiming just before giving the radiation. This may help deliver the radiation even more precisely, which may result in fewer side effects, although more research is needed to prove this.

A variation of IMRT is called *volumetric modulated arc therapy*. It uses a machine that delivers the radiation quickly as it rotates once around the body. This allows each treatment to be given over just a few minutes. Although this can be more convenient for the patient, it hasn’t yet been shown to be more effective than regular IMRT.

Another approach is to place tiny implants into the prostate that send out radio waves to tell the radiation therapy machines where to aim. This lets the machine compensate for movement (like during breathing) and may allow less radiation to go to normal tissues. In theory, this could lower side effects. So far, though, no study has shown side effects to be lower with this approach than with other forms of IMRT. The machines that use this are known as Calypso®.

Stereotactic body radiation therapy (SBRT)

This technique uses advanced image guided techniques to deliver large doses of radiation to a certain precise area, such as the prostate. Because there are large doses of radiation in each dose, the entire course of treatment is given over just a few days.

SBRT is often known by the names of the machines that deliver the radiation, such as Gamma Knife®, X-Knife®, CyberKnife®, and Clinac®.

The main advantage of SBRT over IMRT is that the treatment takes less time (days instead of weeks). Side effects, though, are not better. In fact, one study showed that some side effects were actually worse with SBRT as compared with IMRT in men treated for prostate cancer.

Proton beam radiation therapy

Proton beam therapy focuses beams of protons instead of x-rays 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 release their energy only after traveling a certain distance. This means that proton beam radiation can, in theory, deliver more radiation to the prostate while doing less damage to nearby normal tissues. Proton beam radiation can be aimed with similar techniques to 3D-CRT and IMRT.

Although early results are promising, so far studies have not shown that proton beam therapy is better in the long-run than other types of external beam radiation. Right now, proton beam therapy is not widely available. The machines needed to make protons are very expensive, and they aren't available in many centers in the United States. Proton beam radiation might not be covered by all insurance companies at this time.

Possible side effects of EBRT

Any numbers below used to describe the possible side effects 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: Radiation can irritate the large intestine and rectum and lead to a condition called *radiation proctitis*. This can lead to diarrhea, sometimes with blood in the stool, and rectal leakage. 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 EBRT, but the newer conformal radiation techniques may be less likely to cause these problems.

Bladder problems: Radiation can irritate the bladder and lead to a condition called radiation cystitis. You might need to urinate more often, have a burning sensation while you urinate, and/or find blood in your urine. Bladder problems usually improve over time, but in some men they never go away. About 1 man out of 3 continues to need to urinate more often.

Urinary incontinence: Overall, this side effect is less common than after surgery. The risk is low at first, but it goes up each year for several years after treatment.

Erection problems, including impotence: After a few years, the impotence rate after radiation is about the same as that after 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 EBRT, but some of these men had erection problems before treatment. About half of men who had normal erections before treatment 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 have problems with erections. Impotence may be helped by treatments such as those listed in the surgery section, including erectile dysfunction medicines.

For more about coping with erection problems and other sexuality issues, see our document *Sexuality for the Man With Cancer*.

Feeling tired: Radiation therapy may cause fatigue that may not go away until a few months after treatment stops.

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

Urethral stricture: The tube that carries urine from the bladder out of the body may, rarely, be scarred and narrowed by radiation. This can cause problems with urination, and may require further treatment to open it up again.

Brachytherapy (internal radiation therapy)

Brachytherapy (also called *seed implantation* or *interstitial radiation therapy*) uses small radioactive pellets, or "seeds," each about the size of a grain of rice. These pellets are placed directly into your prostate.

Brachytherapy is generally used only in men with early stage prostate cancer that is relatively slow growing (such as low-grade tumors). 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 it might not be possible to place the seeds into all of the correct locations. Doctors are now looking at ways to get 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 are used to 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 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 lowers 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, the seeds cause 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 an overnight stay 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 higher Gleason score).

Temporary (high dose rate, or HDR) brachytherapy

This is a newer technique. Hollow needles are placed through the skin between the scrotum and anus and 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 2 days. After the last treatment the catheters are removed. For about a week after treatment, you may have some pain or swelling 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 bowel problems, urinary problems, and problems with erections.

Bowel problems: Significant long-term bowel problems (including rectal pain, burning, 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 men who have brachytherapy. This may be 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.

Erection problems: Some studies have found rates of erection problems to be lower after brachytherapy, but other studies have found that the 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.

To learn more about radiation therapy, see the “Radiation Therapy” section of our website, or our document *Understanding Radiation Therapy: A Guide for Patients and Families*.

Cryosurgery for prostate cancer

Cryosurgery (also called *cryotherapy* or *cryoablation*) is sometimes used to treat early stage 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 doctor guides them into the prostate using transrectal ultrasound (TRUS). This type of procedure requires spinal or epidural anesthesia (where the lower half of your body is numbed) or general anesthesia (where you are asleep).

Very cold gases are then passed through the needles, creating ice balls that destroy the prostate gland. To be sure the prostate 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 during the procedure to keep it from freezing. The catheter is kept in place for about 3 weeks afterward to allow the bladder to empty while you recover.

After the procedure, there will be some bruising and soreness in the area where the probes were inserted. You might need to stay in the hospital overnight, but many patients leave the same 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.

Cryosurgery doesn't appear to be as good as radiation for more advanced prostate tumors. In a study comparing cryosurgery to radiation therapy for locally advanced prostate cancer (T2c to T3b tumors), more men in the cryosurgery group had elevated PSA levels (a sign that their cancers had come back) after 8 years than the men in the radiation group.

Current techniques using ultrasound guidance and precise temperature monitoring have only been available for a few years.

For this reason, most doctors do not often use cryosurgery as the first treatment for 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 4 out of 5 men who have cryosurgery. Erectile dysfunction is more common after cryosurgery than after radical prostatectomy. For information on coping with erection problems and other sexuality issues, see our document *Sexuality for the Man With Cancer*.

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.

After cryosurgery, less than 1% of men develop a fistula (an abnormal connection) between the rectum and bladder. This rare but serious problem can allow urine to leak into the rectum and often requires surgery to repair.

Hormone (androgen deprivation) therapy for prostate cancer

Hormone therapy is also called *androgen deprivation therapy* (ADT) or *androgen suppression therapy*. The goal is to reduce levels of male hormones, called *androgens*, in the body, or to prevent them from reaching prostate cancer cells.

The main androgens are testosterone and dihydrotestosterone (DHT). Most of the body's androgens come from the testicles, but the adrenal glands also make a small amount. Androgens stimulate prostate cancer cells to grow. Lowering androgen levels or stopping them from getting into prostate cancer cells often makes prostate cancers shrink or grow more slowly for a time. However, hormone therapy alone does not cure prostate cancer and eventually, it stops helping.

Hormone therapy may be used:

- 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
- Along with radiation therapy as initial treatment if you are at higher risk of the cancer coming back after treatment (based on a high Gleason score, high PSA level, and/or growth of the cancer outside the prostate)
- Before radiation to try to shrink the cancer to make treatment more effective

Several types of hormone therapy can be used to treat prostate cancer. Some lower the levels of testosterone or other androgens (male hormones). Others block the action of those hormones.

Treatments to lower androgen levels

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 most of the androgens (testosterone and DHT) 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 afterward. If wanted, artificial silicone sacs can be inserted into the scrotum. These look much like testicles.

Luteinizing hormone-releasing hormone (LHRH) analogs

These drugs lower the amount of testosterone made by the testicles. Treatment with these drugs is sometimes called *chemical castration* because they lower androgen levels just as well as orchiectomy.

Even though LHRH analogs (also called *LHRH agonists*) cost more than orchiectomy and require more frequent doctor visits, most men choose this method. These drugs allow the testicles to remain in place, but the testicles will shrink over time, and they may even become too small to feel.

LHRH analogs are injected or placed as small implants under the skin. Depending on the drug used, they are given anywhere from once a month up to once a year. The LHRH analogs available in the United States include leuprolide (Lupron®, Eligard®), goserelin (Zoladex®), triptorelin (Trelstar®), and histrelin (Vantas®).

When LHRH analogs are first given, testosterone levels go up 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 have bone pain. If the cancer has spread to the spine, even a short-term increase in tumor growth as a result of the flare 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. (Anti-androgens are discussed further on.)

Luteinizing hormone-releasing hormone (LHRH) antagonists

LHRH antagonists work like LHRH agonists, but they reduce testosterone levels more quickly and do not cause tumor flare like the LHRH agonists do.

Degarelix (Firmagon®) is an LHRH antagonist used to treat advanced prostate cancer. It is given as a monthly injection under the skin and quickly reduces testosterone levels. The most common side effects are problems at the injection site (pain, redness, and swelling) and increased levels of liver enzymes on lab tests. Other side effects are discussed in detail below.

Abiraterone (Zytiga®)

Drugs such as LHRH agonists can stop the testicles from making androgens, but other cells in the body, including prostate cancer cells themselves, can still make small amounts, which may fuel cancer growth. Abiraterone blocks an enzyme called CYP17, which helps stop these cells from making certain hormones, including androgens.

Abiraterone can be used in men with advanced castrate-resistant prostate cancer (cancer that is still growing despite low testosterone levels from LHRH agonists, LHRH antagonists, or orchiectomy). Abiraterone has been shown to shrink or slow the growth of some of these tumors and help some of these men live longer.

This drug is a pill and the most common dose is 4 pills every day. Since this drug doesn't stop the testicles from making testosterone, men who haven't had an orchiectomy need to continue with treatment to stop the testicles from making testosterone (LHRH agonist or antagonist therapy). Because abiraterone lowers the level of other hormones in the body, prednisone (a cortisone-like drug) needs to be taken during treatment as well to avoid the side effects caused by lower levels of these other hormones.

Drugs that stop androgens from working

Anti-androgens

Androgens have to bind to a protein in the cell called an androgen receptor in order to work. Anti-androgens stop androgens from working by binding to the receptors so the androgens can't.

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 in this country. An anti-androgen may be added to treatment if orchiectomy, an LHRH analog, or LHRH antagonist is no longer working by itself. An anti-androgen is sometimes given for a few weeks when an LHRH analog is first started to prevent a tumor flare.

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.

In some men, if hormone therapy including an anti-androgen stops working, the cancer will stop growing 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.

Enzalutamide (Xtandi®)

This drug is a newer type of anti-androgen. When androgens bind to the androgen receptor, the receptor sends a signal for the cells to grow and divide. Enzalutamide (also known as MDV3100) blocks this signal from the androgen receptor to the cell.

In men with castrate-resistant prostate cancer who have already been treated with the chemotherapy drug docetaxel (Taxotere®), enzalutamide has been shown to lower PSA levels, shrink or slow the growth of tumors, and help them live longer. This drug is also being studied to see if it can help men earlier in treatment.

Enzalutamide is a pill, with the most common dose being 4 pills each day. In studies of this drug, men stayed on LHRH agonist treatment, so it isn't clear how helpful this drug would be in men with non-castrate levels of testosterone.

Other androgen-suppressing drugs

Estrogens (female hormones) 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 certain hormones, including androgens, similarly to abiraterone. It is most often used to treat men just diagnosed with advanced prostate cancer who have a lot of cancer in the body, as it offers a quick way to lower testosterone levels. It can also be tried if other forms of hormone therapy are no longer effective.

Ketoconazole can block the production of cortisol, an important steroid hormone in the body. People treated with ketoconazole often need to take a corticosteroid (like hydrocortisone) to prevent the side effects caused by low cortisol levels.

Possible side effects of hormone therapy

Orchiectomy, LHRH analogs, and LHRH antagonists can all cause similar side effects due to changes in the levels of hormones such as testosterone and estrogen. These side effects can include:

- Reduced or absent libido (sexual desire)
- Impotence (erectile dysfunction)
- Shrinking of testicles and penis
- Hot flashes, which may get better or even 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 sharpness
- Loss of muscle mass
- Weight gain
- Fatigue
- Increased cholesterol
- Depression

Some research has suggested that the risk of high blood pressure, diabetes, strokes, heart attacks, and even death from heart disease is higher in men treated with hormone therapy, although not all studies have found this.

Anti-androgens have similar side effects. 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. When these drugs are given to men already being treated with LHRH agonists, diarrhea is the major side effect. Nausea, liver problems, and tiredness can also occur.

Abiraterone does not usually cause major side effects, although it can cause joint or muscle pain, high blood pressure, fluid buildup in the body, hot flashes, upset stomach, and diarrhea.

Enzalutamide can cause diarrhea, fatigue, and worsening of hot flashes. This drug can also cause some neurologic side effects, including dizziness and, rarely, seizures. Men taking this drug are more likely to have problems with falls, which may lead to injuries.

Many side effects of hormone therapy can be prevented or treated. For example:

- Hot flashes can often be helped by treatment with certain antidepressants or other drugs.
- Brief radiation treatment to the breasts can help prevent their enlargement, but it is not effective once breast enlargement has occurred.
- Several different drugs are available to help prevent and treat osteoporosis.
- Depression can be treated by antidepressants and/or counseling.
- Exercise can help reduce many side effects, including fatigue, weight gain, and the loss of bone and muscle mass.

There is growing concern that hormone therapy for prostate cancer may lead to problems with thinking, concentration, and/or memory. But this has not been studied well in men getting hormone therapy for prostate cancer. Studying the possible effects of hormone therapy on brain function is hard, because other factors may also change the way the

brain works. A study has to take all of these factors into account. For example, both prostate cancer and memory problems become more common as men get older. Hormone therapy can also lead to anemia, fatigue, and depression – all of which can affect brain function. Still, hormone therapy does seem to lead to memory problems in some men. These problems are rarely severe, and most often affect only some types of memory. More studies are being done to look at this issue.

To learn more about each of these drugs and many other drugs used in cancer treatment, please see our Guide to Cancer Drugs online, or call us anytime.

Current issues 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 are now looking at these issues. A few of them are discussed here.

Treating early stage cancer: Some doctors have used hormone therapy instead of watchful waiting or active surveillance in men with early (stage I or II) prostate cancer who do not want surgery or radiation. Studies have not found that these men live any longer than those who do not receive any treatment at first, but instead wait until the cancer progresses or symptoms develop. Because of this, hormone treatment is not usually advised for early stage prostate cancer.

Early versus delayed treatment: For men who need (or will eventually need) hormone therapy, such as men whose PSA level is rising after surgery or radiation or men with advanced prostate cancer who do not yet have symptoms, it is not always clear when it is best to start hormone treatment. Some doctors think that hormone therapy works better if it is started as soon as possible, even if a man feels well and is not having any symptoms. Some studies have shown that hormone treatment may slow down the disease and perhaps even lengthen 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 of hormone therapy and the chance that the cancer could become resistant to therapy sooner, treatment should not be started until a man has symptoms from the cancer. Studies looking at this issue are now under way.

Intermittent versus 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. The hope is that giving men a break from androgen suppression will also give them a break from side effects like decreased energy, impotence, hot flashes, and loss of sex drive.

In one form of intermittent therapy, hormone treatment is stopped once the PSA drops to a very low level. If the PSA level begins to rise, the drugs are started again. Another form

of intermittent therapy uses hormone therapy for fixed periods of time – for example, 6 months on followed by 6 months off.

At this time, it isn’t clear that this approach is better than continuous hormone therapy, and it may even be worse in some ways. In one study of men with advanced prostate cancer, it wasn’t clear that intermittent therapy helped men live as long as continuous therapy. The men on intermittent therapy also did not have much improvement in terms of side effects. While they did report fewer problems with impotence and sex drive when looked at 3 months into the study, there was no difference later on.

Combined androgen blockade (CAB): Some doctors treat patients with both androgen deprivation (orchiectomy or an LHRH agonist or antagonist) plus an anti-androgen. Some studies have suggested this may be more helpful than androgen deprivation alone, but others have not. Most doctors are not convinced there's enough evidence that this combined therapy is better than one drug alone when treating metastatic prostate cancer.

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) 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.

"Castrate resistant" vs. "hormone refractory" prostate cancer: These terms are both sometimes used to describe prostate cancers that are no longer responding to hormones, although there is a difference between the two.

"Castrate resistant" means the cancer is still growing even when the testosterone levels are as low as what would be expected if the testicles were removed (called “castrate” levels). Levels this low could be from an orchiectomy, an LHRH agonist, or an LHRH antagonist. Some men may be uncomfortable with this term, but it is specifically meant to refer to these cancers, some of which may still be helped by other forms of hormone therapy, such as the drugs abiraterone and enzalutamide. Cancers that are still responsive to some type of hormone therapy are not completely "hormone refractory" and so that term cannot be used.

"Hormone refractory" refers to prostate cancer that is no longer helped by any type of hormone therapy, including the newer medicines.

Chemotherapy for prostate cancer

Chemotherapy (chemo) 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.

Chemotherapy is sometimes used if prostate cancer has spread outside the prostate gland and hormone therapy isn't working. Chemo is not a standard treatment for early prostate

cancer, but some studies are looking to see if it could be helpful if given for a short time after surgery.

Doctors give chemotherapy in cycles, with each period of treatment followed by a rest period to allow the body time to recover. Each cycle typically lasts for a few weeks.

For prostate cancer, chemo drugs are typically used one at a time. Some of the chemo drugs used to treat prostate cancer include:

- Docetaxel (Taxotere®)
- Cabazitaxel (Jevtana®)
- Mitoxantrone (Novantrone®)
- Estramustine (Emcyt®)
- Doxorubicin (Adriamycin®)
- Etoposide (VP-16)
- Vinblastine (Velban®)
- Paclitaxel (Taxol®)
- Carboplatin (Paraplatin®)
- Vinorelbine (Navelbine®)

In most cases, the first chemo drug given is docetaxel, combined with the steroid drug prednisone. If this drug does not work (or stops working), a newer drug called cabazitaxel is often the next chemo drug tried (although there may be other treatment options as well).

Both of these drugs have been shown to help men live several months longer, on average, than older chemotherapy drugs. They may slow the cancer's growth and also reduce symptoms, resulting in a better quality of life. Still, chemotherapy for prostate cancer is very unlikely to result in a cure.

Possible side effects of chemotherapy

Chemo drugs attack 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
- Diarrhea
- 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)

Most of these side effects 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 help prevent or reduce nausea and vomiting. Other drugs can be given to boost blood cell counts, if needed.

Along with the risks above, some side effects are seen more often with certain chemo drugs. For example:

- Docetaxel and cabazitaxel can sometimes cause severe allergic reactions. Medicines are given before each treatment to help prevent this problem. These drugs can also cause numbness, tingling, or burning sensations in the hands or feet, which is known as *peripheral neuropathy*.
- Mitoxantrone can rarely cause leukemia several years later.
- Estramustine carries an increased risk of blood clots.
- Doxorubicin can weaken the heart muscle over time, so doctors must limit the amount of this drug that is used.

To learn more about chemotherapy, see the “Chemotherapy” section on our website, or our document *Understanding Chemotherapy: A Guide for Patients and Families*.

Vaccine treatment for prostate cancer

Sipuleucel-T (Provenge®) is a cancer vaccine. Unlike traditional vaccines, which boost the body's immune system to prevent infectious diseases, this vaccine boosts the immune system to get it to attack prostate cancer cells in the body.

The vaccine is used to treat advanced prostate cancer that is no longer responding to initial hormone therapy but that is causing few or no symptoms.

This vaccine is made specially for each man – it is not mass produced. To make it, white blood cells (cells of the immune system) are removed from the patient's blood over a few hours while he is hooked up to a special machine. The cells are then sent to a lab, where they are exposed to a protein from prostate cancer cells called *prostatic acid phosphatase* (PAP). The cells are then sent back to the doctor's office or hospital, where they are given back to the patient by infusion into a vein (IV). This process is repeated 2 more times, 2 weeks apart, so that the patient gets 3 doses of cells. In the body, the cells help other immune system cells to attack the prostate cancer.

When used in men with advanced prostate cancer that no longer responds to hormone therapy, the vaccine didn't seem to stop the cancers from growing, but it did help the men live several months longer on average. As with hormone therapy and chemotherapy, this type of treatment has not been shown to cure these cancers.

Studies are now being done to see if this vaccine can help men with less advanced prostate cancer.

Possible side effects of vaccine treatment

Side effects from the vaccine tend to be milder than those from hormone therapy or chemotherapy. Common side effects can include fever, chills, fatigue, back and joint pain, nausea, and headache. These most often start during the cell infusions and last no more than a day or 2. A few men may have more severe symptoms, including problems breathing and high blood pressure, which usually improve after treatment.

Preventing and treating prostate cancer spread to bone

If prostate cancer grows outside of the prostate gland itself, it may first grow into nearby tissues or spread to nearby lymph nodes. After this, prostate cancer nearly always spreads to the bones next. Spread of cancer to the bones can be painful and can also result in other problems, such as fractures (breaks) or high blood calcium levels, which can be dangerous or even life threatening.

Preventing or slowing the spread of prostate cancer to the bones is a major goal of treatment if the cancer has grown outside of the prostate. If the cancer has already reached the bones, controlling or relieving pain and other complications is also a very important part of treatment.

Previously described treatments, such as hormone therapy, chemotherapy, and vaccines may help with this, but other treatments more specifically target cancer spread to the bones and the problems it may cause.

Bisphosphonates

Bisphosphonates are a group of drugs that can help relieve pain and high calcium levels caused by cancer that has spread (metastasized) to the bones. These drugs may also slow the growth of the metastases and help delay or prevent fractures. Bisphosphonates can also help strengthen bones in men who are receiving hormone therapy.

These drugs work by slowing down cells called *osteoclasts*. These cells normally break down the hard mineral structure of bones to help keep them healthy. But osteoclasts often become overactive when prostate cancer cells spread to the bones, which can cause problems.

For prostate cancer, the most commonly used bisphosphonate is zoledronic acid (Zometa®). This drug is approved to treat bone metastases from prostate cancer. It is given as an intravenous (IV) injection, usually once every 3 or 4 weeks. Men given this drug are advised to take a supplement containing calcium and vitamin D to prevent problems with low calcium levels.

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 that has spread to bone.

Bisphosphonates can also be used to treat osteoporosis (thinning and weakening of bones). Some men with prostate cancer develop this as a result of hormone therapy.

Bisphosphonates can have side effects, including flu-like symptoms and bone or joint pain. They can also lead to kidney problems, so patients with poor kidney function may not be able to be treated with these medicines.

A rare but very serious side effect of bisphosphonates is osteonecrosis of the jaw (ONJ). With this condition, part of the jaw bone loses its blood supply and dies. This can lead to tooth loss and infections or open sores of the jaw bone that won't heal and are hard to treat. Some people develop ONJ after dental work (such as having a tooth pulled) is done while on this medicine. Many cancer doctors advise patients to have a dental checkup and have any tooth or jaw problems treated before they start taking a bisphosphonate. Maintaining good oral hygiene by flossing and brushing, making sure that dentures fit properly, and having regular dental checkups may also help prevent this condition.

Denosumab

Denosumab (Xgeva®, Prolia®) is another drug that can help when prostate cancer spreads to bone. Like the bisphosphonates, denosumab also blocks bone cells called *osteoclasts*, but it does so in a different way.

In men whose cancer has already spread to the bones, denosumab can help prevent or delay problems like fractures. Studies have shown that it seems to work a bit better than zoledronic acid. It may also be helpful if zoledronic acid is no longer working.

In men with no obvious cancer spread to the bones but with rising PSA levels despite hormone therapy, denosumab may help slow the spread of the cancer to the bones. But it's not clear if it will help men live longer.

This drug is given as an injection under the skin every 4 weeks. Men given this drug are often urged to take a supplement containing calcium and vitamin D to prevent problems with low calcium levels.

Common side effects include nausea, diarrhea, and feeling weak or tired. Like the bisphosphonates, denosumab can also cause ONJ, so doctors recommend taking the same precautions (such as having tooth and jaw problems treated before starting the drug).

Corticosteroids

Some studies suggest that corticosteroid drugs (such as prednisone and dexamethasone) can help relieve bone pain in some men. They also can help lower PSA levels.

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

Radiopharmaceuticals are drugs that contain radioactive elements. They are injected into a vein and settle in areas of the bones with active turnover (like those containing cancer spread). Once there, the radiation they give off kills cancer cells.

Right now, there are 3 radiopharmaceuticals that can be used to treat prostate cancer spread to bone:

- Strontium-89 (Metastron®)
- Samarium-153 (Quadramet®)
- Radium- 223 (Xofigo®, formerly called Alpharadin)

These drugs can be used to treat bone metastases when prostate cancer has spread to many bones. Unlike external beam radiation, this treatment allows all the bones affected by cancer to be treated at the same time.

Although all 3 of these drugs can help relieve pain caused by bone metastases, only radium-223 has been shown to help prostate cancer patients who only have cancer spread in their bones live longer. For these patients, radium-223 may be an early part of treatment.

The major side effect of these drugs 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. Other side effects have also been seen, so ask your doctor what you can expect.

Pain medicines

When properly prescribed, pain medicines (ranging from ibuprofen or acetaminophen to stronger opioids like morphine) are very effective. You may worry about addiction with opioids, but this is almost never a problem if the drug is being used as directed to treat cancer pain. Symptoms such as drowsiness and constipation are likely but can usually be treated by changing the dose or by adding other medicines.

If you have bone pain from prostate cancer, it is very important that it is treated effectively. This will help you feel better and allow you to focus on the people and activities that are most important to you. 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. For more on managing pain, see the “Cancer-related Pain” section of our website or our document *Guide to Controlling Cancer Pain*.

Clinical trials for prostate cancer

You may 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 choosing 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 carefully controlled research studies that are done with patients who volunteer for them. They are done to get a closer look at promising new treatments or procedures.

If you would like to take part in a clinical trial, you should start by asking your doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service for a list of clinical trials that meet your medical needs. You can reach this service at 1-800-303-5691 or on our website at http://clinicaltrials.cancer.org. 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 website at www.cancer.gov/clinicaltrials.

There are requirements you must meet to take part in any clinical trial. If you do qualify for a clinical trial, it is up to you whether or not to enter (enroll in) it.

Clinical trials are one way to get state-of-the art cancer treatment. Sometimes they may be the only way to get some newer treatments. They are also the only way for doctors to learn better methods to treat cancer. Still, they are not right for everyone.

You can get a lot more information on clinical trials in our document called *Clinical Trials: What You Need to Know*. You can read it on our website or call our toll-free number (1-800-227-2345) and have it sent to you.

Complementary and alternative therapies for prostate cancer

When you have cancer you are likely to hear about ways to treat your cancer or relieve symptoms that your doctor hasn't mentioned. Everyone from friends and family to Internet groups and websites may offer ideas for what might help you. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

What exactly are complementary and alternative therapies?

Not everyone uses these terms the same way, and they are used to refer to many different methods, so it can be confusing. We use *complementary* to refer to treatments that are used *along with* your regular medical care. *Alternative* treatments are used *instead of* a doctor's medical treatment.

Complementary methods: Most complementary treatment methods are not offered as cures for cancer. Mainly, they are used to help you feel better. Some methods that are used along with regular treatment are meditation to reduce stress, acupuncture to help relieve pain, or peppermint tea to relieve nausea. Some complementary methods are known to help, while others have not been tested. Some have been proven not be helpful, and a few have even been found harmful.

Alternative treatments: Alternative treatments may be offered as cancer cures. These treatments have not been proven safe and effective in clinical trials. Some of these methods may pose danger, or have life-threatening side effects. But the biggest danger in most cases is that you may lose the chance to be helped by standard medical treatment. Delays or interruptions in your medical treatments may give the cancer more time to grow and make it less likely that treatment will help.

Finding out more

It is easy to see why people with cancer think about alternative methods. You want to do all you can to fight the cancer, and the idea of a treatment with few or no side effects sounds great. Sometimes medical treatments like chemotherapy can be hard to take, or

they may no longer be working. But the truth is that most of these alternative methods have not been tested and proven to work in treating cancer.

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

- Look for "red flags" that suggest fraud. Does the method promise to cure all or most cancers? Are you told not to have regular medical treatments? Is the treatment a "secret" that requires you to visit certain providers or travel to another country?
- Talk to your doctor or nurse about any method you are thinking about using.
- Contact us at 1-800-227-2345 to learn more about complementary and alternative methods in general and to find out about the specific methods you are looking at.

The choice is yours

Decisions about how to treat or manage your cancer are always yours to make. If you want to use a non-standard treatment, learn all you can about the method and talk to your doctor about it. You can also read more on the “Complementary and Alternative Medicine” section of our website or call us to ask about any treatment you’re interested in. With good 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

For most men who are diagnosed with prostate cancer, the cancer is found while it is still at an early stage. These men often have several treatment options to consider.

If you have early stage prostate cancer, there are many important factors to take into account before deciding on a treatment, such as your age and general health, and the likelihood that the cancer will cause problems for you. You should also think about the possible side effects of treatment and how bothersome they would probably be for you. Some men, for example, may want to avoid possible side effects such as incontinence or impotence for as long as possible. 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 (low-grade), 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 active surveillance, 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 all 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.

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 their effectiveness and possible side effects is very difficult, if not impossible.

Such a complex decision is often hard to make by yourself. You may find it helps to talk with your family and friends before making a decision. You might also find that speaking with other men who have faced or are currently facing the same issues is useful. The American Cancer Society and other organizations offer support programs that 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- 227-2345 or see the “Find Support Programs and Services” section of our website. It's important to note that each man's experience with prostate cancer is different. Just because someone you know had a good (or bad) experience with a certain type of treatment doesn't 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.

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/active surveillance, 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? (Some treatments are more likely to cause certain side effects than others.)
- 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, so it's important to take your time and decide which option is right for you.

The information in the following sections describes the main treatment options available for prostate cancer in different situations.

Initial treatment of prostate cancer by stage

The stage of your cancer is one of the most important factors in choosing the best way to treat it. The "How is prostate cancer staged?" section explains how prostate cancer is staged, based on the extent of the cancer (using T, N, and M categories) and the PSA level and Gleason score at the time of diagnosis.

But keep in mind that other factors, such as a man's age, overall health, and life expectancy must also be taken into account when looking at treatment options.

In fact, many doctors determine a man's possible treatment options based not just on the stage, but on the risk of cancer coming back after the initial treatment and on a man's life expectancy.

You may want to ask your doctor what factors he or she is considering when discussing your treatment options. Some doctors might recommend options that are different from those listed here.

Stage I

These prostate cancers are small (T1 or T2a) and have not grown out of the prostate. They have low Gleason scores (6 or less) and low PSA levels (less than 10). 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 that may limit their lifespan, active surveillance is often recommended.

For men who wish to start treatment, radiation therapy (external beam or brachytherapy) or radical prostatectomy may be options.

Men who are younger and healthy may consider active surveillance (knowing that they may later need to be treated), radical prostatectomy, or radiation therapy (external beam or brachytherapy).

Stage II

Stage II cancers have not yet grown outside of the prostate gland, but are larger, have higher Gleason scores, and/or have higher PSA levels than stage I tumors. 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, active surveillance 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 a few months after surgery.
- External beam radiation only*
- Brachytherapy only*
- Brachytherapy and external beam radiation combined*
- Taking part in a clinical trial of newer treatments

*All of 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 grown outside of the prostate capsule but have not reached the bladder or rectum (T3). They have not spread to lymph nodes (N0) or distant organs (M0). These cancers are more likely to come back (recur) after treatment than earlier stage tumors.

Treatment options at this stage may include:

- External beam radiation plus hormone therapy

- External beam radiation plus brachytherapy, possibly with a short course of hormone therapy
- Radical prostatectomy in selected cases (often with removal of the pelvic lymph nodes). This may be followed by radiation therapy.

Men who have other medical problems may be given less aggressive treatment such as hormone therapy (by itself) or even active surveillance.

Taking part in a clinical trial of newer treatments is also an option for many men with stage III prostate cancer.

Stage IV

Stage IV cancers have already spread to nearby areas such as the bladder or rectum (T4), to nearby lymph nodes (N1), or to distant organs such as the bones (M1). A few T4 cancers may be curable using some of the same treatments for stage III cancers above. But most stage IV cancers cannot be cured with standard treatment.

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
- Treatments aimed at bone metastases, such as denosumab (Xgeva), a bisphosphomate like zoledronic acid (Zometa), or a radiopharmaceutical such as strontium-89, samarium-153 or radium-223.
- Chemotherapy
- Active surveillance (for those who have another serious illness)
- Taking part in a clinical trial of newer treatments

Treatment of stage IV prostate cancer may also include treatments to help prevent or relieve symptoms such as bone pain.

Following PSA levels during and after treatment

The prostate-specific antigen (PSA) level is often a good indicator of how effective treatment is or has been. 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.

Before starting treatment, you might want to ask your doctor what he or she expects your PSA level to be during and after treatment, and what levels might be concerning. But it's important to realize that the PSA level is only one part of the overall picture. Other factors may also play a role in determining if cancer is still present or if it is growing.

It's also important to know that PSA levels may fluctuate a bit on their own in some cases. Many men being treated for prostate cancer are very concerned about even very small changes in their PSA levels. The blood PSA level is an important tool to monitor the cancer, but not every rise in PSA necessarily means that the cancer is growing and requires treatment right away. To help avoid possibly unnecessary anxiety, be sure you understand what level of change in PSA your doctor might consider to be a cause for concern.

During active surveillance

If you choose active surveillance, your PSA level will be monitored closely (most likely along with other tests) to help decide whether the cancer is growing and if other types of treatment should be considered. (See the section "Expectant management (watchful waiting) and active surveillance" for more details.)

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.

Blood tests to detect PSA have become much more sensitive in recent years – so sensitive that they can detect very small amounts of PSA. This would seem to be a good thing, but 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. 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.

Having a detectable PSA level after surgery does not always mean that you still have cancer. If you have a low PSA level that is not rising, it could mean that you just have some benign prostate cells still in your body.

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 from after 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 if the PSA rises more than 2 (ng/mL) above the lowest level it reached, further treatment should be considered, but it's not clear if all doctors agree with this.

There is also a phenomenon called a "PSA bounce" that sometimes happens after brachytherapy. 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.

During treatment for advanced prostate cancer

When treatments such as hormone therapy, chemotherapy, or vaccine therapy are used for more advanced prostate cancer, the PSA level can help indicate how well the treatment is working or when it might be time to try a different form of treatment.

Treatments should lower the PSA level (at least at first), although in some cases they may just help keep it from rising further, or even just slow the rise. Of course, other factors, such as whether you are having symptoms from your cancer and whether it is growing based on imaging tests, are also important when deciding if it might be time to change treatments.

If the cancer has spread outside the prostate, the actual PSA level is often not as important as whether it changes, and how quickly it changes. The PSA level itself does not predict whether or not a man will have symptoms or how long he will live. Many men have very high PSA values and feel just fine. Other men have low values and have symptoms.

Prostate cancer that remains or recurs after treatment

If the prostate-specific antigen (PSA) level shows that the prostate cancer has not been cured or has come back (recurred) after an initial attempt to cure it, further treatment may be an option. Follow-up therapy will depend on where the cancer is thought to be located and what treatment(s) you have already had. Imaging tests such as CT, MRI, or bone scans may be done to get a better idea about where the cancer may be.

Cancer that is still in or around the prostate

If the cancer is still thought to be localized to the area of the prostate, a second attempt to try to cure the cancer may be possible. If you've had a radical prostatectomy, radiation therapy may be an option, sometimes along with hormone therapy.

If your first treatment was radiation, treatment options may include cryosurgery or radical prostatectomy, but when radical prostatectomy is done after radiation, it does carry a higher risk for side effects such as incontinence. Repeating radiation therapy is usually not an option because of the increased potential for serious side effects, although in some cases brachytherapy maybe an option as a second treatment.

Cancer that has spread

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.

When prostate cancer has spread to other parts of the body (including the bones), hormone therapy is probably the most effective treatment, but it isn't likely to cure the cancer and at some point it will stop working. Usually the first treatment is a luteinizing hormone-releasing hormone **(**LHRH) analog or antagonist (or orchiectomy). If this stops working, an anti-androgen may be added. Other treatments aimed at bone metastases may be used as well.

Keep in mind 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 for low-grade prostate cancer, 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.

How quickly the PSA goes up can help predict how soon the cancer will show up in distant sites and cause problems. If the PSA is going up very quickly, some doctors may recommend that you begin treatment with hormone therapy even before the cancer can be seen on tests or causes problems.

Castrate-resistant and hormone-refractory prostate cancer

Hormone therapy is often very effective at shrinking or slowing the growth of prostate cancer that has spread, but it nearly always loses its effectiveness over time. Doctors use different terms to describe cancers that are no longer responding to hormones.

- **Castrate-resistant prostate cancer (CRPC)** is cancer that is still growing despite the fact that hormone therapy (either an orchiectomy or an LHRH agonist or

antagonist) is keeping the testosterone in the body at very low, "castrate" levels. The cancer may still respond to other forms of hormone therapy, though.

- **Hormone-refractory prostate cancer (HRPC)** is cancer that is no longer helped by any form of hormone therapy.

Men whose prostate cancer is still growing despite initial hormone therapy now have many more treatment options than they had even a few years ago.

If an anti-androgen drug has not been tried as part of the initial hormone therapy, it is often added at this time. If a man is already getting an anti-androgen but the cancer is still growing, stopping the anti-androgen (while continuing other hormone treatments) actually seems to help in some cases.

Other forms of hormone therapy may also be helpful for a time, especially if the cancer is causing few or no symptoms. These include abiraterone (Zytiga), ketoconazole, estrogens (female hormones), and corticosteroids. The newer hormone therapy drug enzalutamide (Xtandi) may be useful in this situation as well, although doctors are still studying this.

Another option for men whose cancer is causing few or no symptoms is the prostate cancer vaccine sipuleucel-T (Provenge). This may not lower PSA levels, but can help men live longer.

For cancers that are no longer responding to initial hormone therapy and are causing symptoms, several options may be available. Chemotherapy with the drug docetaxel (Taxotere) is often the first choice because it has been shown to help men live longer, as well as reduce any pain they are having.

If docetaxel does not work or stops working, cabazitaxel (Jevtana) or other chemo drugs may help. Another option may be a different type of hormone therapy, such as abiraterone (if it hasn’t been tried yet) or enzalutamide.

Bisphosphonates or the newer drug denosumab 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. A radiopharmaceutical such as strontium, samarium, or radium 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 and entire care team know about 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 our document *Advanced Cancer*.

There are several promising new medicines now being tested against prostate cancer, including vaccines, monoclonal antibodies, and other types of targeted drugs. 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 prostate cancer 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 website (www.nccn.org).

The NCI provides treatment guidelines via its telephone information center (1-800-4-CANCER) and its website (www.cancer.gov). Detailed guidelines intended for use by cancer care professionals are also available on 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?
- Are there other types of doctors I should talk to before deciding on treatment?
- What is the clinical stage and Gleason score (grade) of my cancer? What do those mean in my case? Does this make me a low-risk, intermediate-risk or high-risk patient?
- What is my expected survival rate based on clinical stage, grade, and various treatment options?
- Should I consider active surveillance 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 risks or side effects should I 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?
- How quickly do I need to decide on treatment?
- What should I do to be ready for treatment?
- How long will treatment last? What will it involve? Where will it be done?
- How would treatment affect my daily activities?
- What are the chances my cancer will come back with the treatment programs we have discussed? What would be our next step if this happened?
- What type of follow-up will I need after treatment?
- Where can I find more information and support?

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 or activity 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 clinical trials for which you may qualify.

What happens after treatment for prostate cancer?

For most men with prostate cancer, treatment may remove or destroy the cancer. Completing treatment can be both stressful and exciting. You may be relieved to finish treatment, but find it hard not to worry about cancer growing or coming back. (When cancer comes back after treatment, it is called *recurrence*.) This is a very common concern in people who have had cancer.

It may take a while before your fears lessen. But it may help to know that many cancer survivors have learned to live with this uncertainty and are leading full lives. Our document *Living With Uncertainty: The Fear of Cancer Recurrence* gives more detailed information on this.

For other men, the cancer may return or may never go away completely. These men may get treatment with hormone therapy or other therapies to help keep the cancer in check

for as long as possible. Learning to live with cancer as a more of a chronic disease can be difficult and very stressful. It has its own type of uncertainty. Our document *When Cancer Doesn't Go Away* talks more about this.

Follow-up care

If you have completed treatment, your doctors will still want to watch you closely. It is very important to go to all of your follow-up appointments. During these visits, your doctors will ask questions about any problems you may have and may do exams and lab tests or imaging tests to look for signs of cancer or treatment side effects.

Your doctor should give you a follow-up plan. This plan usually includes regular doctor visits and PSA blood tests, with digital rectal exams if your prostate hasn't been removed. These 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.

Almost any cancer treatment can have side effects. Some may last for a few weeks to months, but others can last the rest of your life. This is the time for you to talk to your cancer care team about any changes or problems you notice and any questions or concerns you have.

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 "Prostate cancer that remains or recurs after treatment." For more general information on dealing with a recurrence, you may also want to see the document *When Your Cancer Comes Back: Cancer Recurrence*.

Seeing a new doctor

At some point after your cancer diagnosis and treatment, you may find yourself seeing a new doctor who does not know anything about your medical history. It is important that you be able to give your new doctor the details of your diagnosis and treatment. Make sure you have this information handy:

- A copy of your pathology report(s) from any biopsies or surgeries
- If you had surgery, a copy of your operative report(s)
- If you had radiation therapy, a copy of your treatment summary

- Copies of imaging tests (CT or MRI scans, etc.), which can usually be stored on a CD, DVD, etc.
- If you stayed in the hospital, a copy of the discharge summary that doctors prepare when patients are sent home
- If you had hormone therapy, chemotherapy, or other drug treatments, a list of your drugs, drug doses, and when you took them

The doctor may want copies of this information for his records, but always keep copies for yourself.

It is also important to keep your health insurance. Tests and doctor visits cost a lot, and even though no one wants to think of their cancer coming back, this could happen.

Lifestyle changes after having prostate cancer

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 choices to help you stay healthy and feel as well as you can. This can 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 start during cancer treatment.

Making healthier choices

For many people, a diagnosis of cancer helps them focus on their health in ways they may not have thought much about in the past. Are there things you could do that might make you healthier? Maybe you could try to eat better or get more exercise. Maybe you could cut down on the alcohol, or give up tobacco. Even things like keeping your stress level under control may help. Now is a good time to think about making changes that can have positive effects for the rest of your life. You will feel better and you will also be healthier.

You can start by working on those things that worry you most. 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 for information and support. This tobacco cessation and coaching service can help increase your chances of quitting for good.

Eating better

Eating right can be hard for anyone, but it can get even tougher during and after cancer treatment. Treatment may change your sense of taste. Nausea can be a problem. You may not feel like eating and lose weight when you don't want to. Or you may have gained weight that you can't seem to lose. All of these things can be very frustrating.

If treatment caused weight changes or eating or taste problems, do the best you can and keep in mind that these problems usually get better over time. You may find it helps to eat small portions every 2 to 3 hours until you feel better. You may also want to ask your cancer team about seeing a dietitian, an expert in nutrition who can give you ideas on how to deal with these treatment side effects.

One of the best things you can do after cancer treatment is put healthy eating habits into place. You may be surprised at the long-term benefits of some simple changes, like increasing the variety of healthy foods you eat. Getting to and staying at a healthy weight, eating a healthy diet, and limiting your alcohol intake may lower your risk for a number of types of cancer, as well as having many other health benefits.

For more information, see our document *Nutrition and Physical Activity During and After Cancer Treatment: Answers to Common Questions*.

Rest, fatigue, and exercise

Extreme tiredness, called *fatigue*, is very common in people treated for cancer. This is not a normal tiredness, but a "bone-weary" exhaustion that doesn't get better with rest. For some people, fatigue lasts a long time after treatment, and can make it hard for them to exercise and do other things they want to do. But exercise can help reduce fatigue. Studies have shown that patients who follow an exercise program tailored to their personal needs feel better physically and emotionally and can cope better, too.

If you were sick and not very active during treatment, it is normal for your fitness, endurance, and muscle strength to decline. Any plan for 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 twice a week. If you haven't exercised in a few years, you will have to start slowly – maybe just by taking short walks.

Talk with your health care team before starting anything. Get their opinion about your exercise plans. Then, try to find an exercise buddy so 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, you will need to balance activity with rest. It is OK to rest when you need to. Sometimes it's really hard for people to allow themselves to rest when they are used to working all day or taking care of a household, but this is not the time to push yourself too hard. Listen to your body and rest when you need to. (For more information on fatigue and other side effects, please see the “Physical Side Effects” section of our website or “Additional resources for prostate cancer” to get a list of available information.)

Keep in mind exercise can improve your physical and emotional health.

- It improves your cardiovascular (heart and circulation) fitness.

- Along with a good diet, it will help you get to and stay at a healthy weight.
- It makes your muscles stronger.
- It reduces fatigue and helps you have more energy.
- It can help lower anxiety and depression.
- It can make you feel happier.
- It helps you feel better about yourself.

And long term, we know that getting regular physical activity plays a role in helping to lower the risk of some cancers, as well as having other health benefits.

Can I lower my risk of the cancer progressing or coming back?

Most people want to know if there are specific lifestyle changes they can make to reduce their risk of cancer progressing or coming back. Unfortunately, for most cancers there is little solid evidence to guide people. This doesn't mean that nothing will help – it's just that for the most part this is an area that hasn't been well studied. Most studies have looked at lifestyle changes as ways of preventing cancer in the first place, not slowing it down or preventing it from coming back.

Some recent research has suggested that men who exercise regularly after treatment may live longer than those who don't. It's not clear exactly how much activity might be needed, but more seems to be better. More vigorous activity may also be more helpful than less vigorous activity. Further studies are needed to follow up on these findings.

Other recent research has suggested that men who smoke are more likely to have their prostate cancer recur than men who don't smoke. More research is needed to see if quitting smoking is helpful, although quitting is already known to have a number of other health benefits.

Adopting other healthy behaviors such eating well and getting to or staying at a healthy weight may also help, but no one knows for sure. However, we do know that these types of changes can have positive effects on your health that can extend beyond your risk of prostate or other cancers.

How does having prostate cancer affect your emotional health?

During and after treatment, you may find yourself overcome with many different emotions. This happens to a lot of people.

You may find yourself thinking about death and dying. Or maybe you're more aware of the effect the cancer has on your family, friends, and career. You may take a new look at your relationships with those around you. Unexpected issues may also cause concern. For instance, as you feel better and have fewer doctor visits, you will see your health care team less often and have more time on your hands. These changes can make some people anxious.

Almost everyone who has been through cancer can benefit from getting some type of 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 one-on-one counselors. 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 good for you to try to deal with everything on your own. And your friends and family may feel shut out if you do not 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 1-800-227-2345 and we can put you in touch with a group or resource that may work for you. You can also read our document *Distress in People with Cancer* or see the "Emotional Side Effects" section of our website for more information.

If prostate cancer treatment stops working

If cancer keeps growing or comes back after one kind of treatment, it is possible that another treatment plan might still cure the cancer, or at least shrink it enough to help you live longer and feel better. But when a person has tried many different treatments and the cancer has not gotten any better, the cancer tends to become resistant to all treatment. If this happens, it's important to weigh the possible limited benefits of a new treatment against the possible downsides. Everyone has their own way of looking at this.

This is likely to be the hardest part of your battle with cancer – when you have been through many medical treatments and nothing's working anymore. Your doctor may offer you new options, but at some point you may need to consider that treatment is not likely to improve your health or change your outcome or survival.

If you want to continue to get treatment for as long as you can, you need to think about the odds of treatment having any benefit and how this compares to the possible risks and side effects. In many cases, your doctor can estimate how likely it is the cancer will respond to treatment you are considering. For instance, the doctor might say that more treatment might have less than a 1 in 100 chance of working. Some people are still tempted to try this. But it is important to think about and understand your reasons for choosing this plan.

No matter what you decide to do, you need to feel as good as you can. Make sure you are asking for and getting treatment for any symptoms you might have, such as nausea or pain. This type of treatment is called *palliative care*.

Palliative care helps relieve symptoms, but is not expected to cure the disease. It can be given along with cancer treatment, or can even be cancer treatment. The difference is its purpose - the main purpose of palliative care is to improve the quality of your life, or help you feel as good as you can for as long as you can. Sometimes this means using drugs to help with symptoms like pain or nausea. Sometimes, though, the treatments used to control your symptoms are the same as those used to treat cancer. For instance, radiation might be used to help relieve bone pain caused by cancer that has spread to the bones. Or chemo might be used to help shrink a tumor and keep it from blocking the bowels. But this is not the same as treatment to try to cure the cancer. You can learn more about the changes that occur when curative treatment stops working, and about planning ahead for yourself and your family, in our documents *Nearing the End of Life* and *Advance Directives*.

At some point, you may benefit from hospice care. This is special care that treats the person rather than the disease; it focuses on quality rather than length of life. Most of the time, it is given at home. Your cancer may be causing problems that need to be managed, and hospice focuses on your comfort. You should know that while getting hospice care often means the end of treatments such as chemo and radiation, it doesn't mean you can't have treatment for the problems caused by your cancer or other health conditions. In hospice the focus of your care is on living life as fully as possible and feeling as well as you can at this difficult time. You can learn more about hospice in our document called *Hospice Care*.

Staying hopeful is important, too. 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. Pausing at this time in your cancer treatment gives you a chance to refocus on the most important things in your life. Now 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. Though the cancer may be beyond your control, there are still choices you can make.

What’s new in prostate cancer research and treatment?

Research into the causes, prevention, detection, and treatment of prostate is going on 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. This research will help provide answers about the genetic changes that lead to prostate cancer. This could make it possible to design medicines to target 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.

Recently, a mutation in a gene called *HOXB13* has been linked to early onset prostate cancer that runs in families. This mutation is rare, though, found in less than 2% of the men with prostate cancer that were studied.

The *HOXB13* gene and most of the genes that have been studied so far are from chromosomes that are inherited from both parents. Some research has 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.

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 in the near future. For example, the product of a gene 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 active surveillance.

Prevention

Researchers continue to look for foods (or substances in them) that can help lower prostate cancer risk. Scientists have found some substances in tomatoes (lycopenes) and soybeans (isoflavones) that might 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 have suggested that certain vitamin and mineral supplements (such as vitamin E and selenium) might lower prostate cancer risk. But a large study of this issue, called the Selenium and Vitamin E Cancer Prevention Trial (SELECT), found that neither vitamin E nor selenium supplements lowered prostate cancer risk after daily use for about 5 years. In fact, men taking the vitamin E supplements were later found to have a slightly higher risk of prostate cancer.

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. Overall though, studies have not found that vitamin D protects against prostate cancer.

Many people assume that vitamins and other natural substances cause no harm, but recent research has shown that high doses may be harmful, including those supplements marketed specifically for prostate cancer. For example, one study found that men who take more than 7 multivitamin tablets per week may have an increased risk of developing advanced prostate cancer. Another study showed a higher risk of prostate cancer in men who had high blood levels of omega-3 fatty acids. Fish oil capsules, which some people take to help with their heart, contain large amounts of omega-3 fatty acids.

Scientists have also tested certain hormonal medicines called *5-alpha reductase inhibitors* as a way of reducing prostate cancer risk. The results of these studies were discussed in the section "Can prostate cancer be prevented?"

Early detection

Doctors agree that the prostate-specific antigen (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. Early results have been promising, but these and other new tests are not yet available outside of research labs and will need more study before they are widely used to test for prostate cancer.

Other new tests being studied are urine tests. One test, called Progensa®, looks at the level of prostate cancer antigen 3 (PCA3) in the urine. The higher the level, the more likely that prostate cancer is present. In studies, it was used along with the PSA test.

Another test looks for an abnormal gene change called *TMPRSS2:ERG* in prostate cells. The cells to be tested are found in urine collected after a rectal exam. This gene change is found in about half of all localized prostate cancers. It is rarely found in the cells of men

without prostate cancer. Studies are under way to develop this into a test for early detection of prostate cancer.

Diagnosis

Doctors doing 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 newer approach is to measure blood flow within the gland using a technique called *color Doppler ultrasound*. (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. This test is currently only available as a part of a clinical trial.

Doctors are also studying whether MRI can be used to help guide prostate biopsies in men who previously had negative TRUS-guided biopsies but when the doctor still suspects cancer.

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.

A newer type of positron-emission tomography PET scan that uses radioactive carbon acetate instead of labeled glucose (sugar) may also be helpful in detecting prostate cancer in different parts of the body, as well as helping to determine if treatment has been effective. Studies of this technique are now in progress.

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 nerve grafts to replace cut nerves and restore potency. These grafts could be nerves removed from other parts of the body or something artificial. 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 "Radiation therapy for prostate cancer," 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), intensity modulated radiation therapy (IMRT), and proton beam radiation allow doctors to treat only the prostate gland and avoid radiation to normal tissues as much as possible. These methods are expected to increase the effectiveness of radiation therapy while reducing the side effects. Studies are being done to find out which radiation techniques are best suited for specific groups of patients with prostate cancer. 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 early stage cancers

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 after radiation therapy in cases where it was not successful.

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

Nutrition and lifestyle changes

One early study has found that in men with a rising PSA level after surgery or radiation therapy, drinking pomegranate juice seemed to slow the time it took the PSA level to double. Larger studies are now trying 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.

Another study 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 diet (no meat, fish, eggs, or dairy products) 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 if 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.

A recent study showed that giving soy supplements after surgery (radical prostatectomy) for prostate cancer did not lower the risk of the cancer coming back.

Hormone therapy

Several newer forms of hormone therapy have been developed in recent years. Some of these may be helpful even if standard forms of hormone therapy are no longer working.

Some examples include abiraterone (Zytiga) and enzalutamide (Xtandi), which described in the section "Hormone therapy for prostate cancer."

Another new drug being studied, known as *orteronel*, works in a similar way to abiraterone. This drug may target CYP17 more precisely, which may do away with the need for taking a steroid drug such as prednisone along with treatment. Orteronel is only available in clinical trials at this time.

5-alpha reductase inhibitors, such as finasteride (Proscar) and dutasteride (Avodart), are drugs that block the conversion of testosterone to the more active dihydrotestosterone (DHT). These drugs are normally used to shrink the prostate in men with benign prostatic hyperplasia. They are also being studied to treat prostate cancer, either to supplement active surveillance or if the PSA level rises after prostatectomy.

Chemotherapy

Studies in recent years have shown that many chemotherapy drugs can affect prostate cancer. Some, such as docetaxel (Taxotere) and cabazitaxel (Jevtana) have been shown to help men live longer. Other new chemo drugs and combinations of drugs are now being studied.

Immunotherapy

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. An example of this type of vaccine is sipuleucel-T (Provenge), which has received FDA approval.

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. Early results with this vaccine have been promising.

Several other prostate cancer vaccines are also in development.

Other drugs

A drug called ipilimumab (Yervoy) targets certain white blood cells that help control the immune system. This drug is used to treat advanced melanoma, and is being tested in men with advanced prostate cancer.

Targeted therapy drugs

Targeted therapy is a newer type of cancer treatment that uses drugs or other substances to identify and attack cancer cells while doing little damage to normal cells. These therapies attack the cancer cells' inner workings -- the programming that makes them different from normal, healthy cells. Each type of targeted therapy works differently, but all alter the way a cancer cell grows, divides, repairs itself, or interacts with other cells.

Cabozantinib (Cometriq™, also known as XL184) is a new drug that targets the MET protein, as well as having an effect on angiogenesis by targeting the VEGFR protein. In early studies, this drug was found to make bone tumors get smaller or even go away on imaging scans in many men whose prostate cancer was no longer responding to hormones. Cabozantinib also helped stop tumor growth (outside the bones) and improved pain. The effect lasted an average of about 6 months. It’s not yet clear if the drug can help men live longer.

Angiogenesis inhibitors

Growth of prostate cancer tumors depends on growth of new 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 have been tested in clinical trials. One of these is thalidomide (Thalomid®), which has been approved by the FDA to treat patients with multiple myeloma. It was combined with chemotherapy in an early phase study of men with advanced prostate cancer. It has also been studied to see

if it could help hormone therapy work better. While promising, this drug can cause major side effects, including nerve damage and serious blood clots.

Treating spread of cancer to the bones

Doctors are 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 a CT scan 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. RFA has been used for many years to treat tumors in other organs such as the liver, but its use in treating bone pain is still fairly new. Still, early results are promising.

Additional resources for prostate cancer

More information from your American Cancer Society

Here is more information you might find helpful. You also can order free copies of our documents from our toll-free number, 1-800-227-2345, or read them on our website, www.cancer.org.

Living with cancer

After Diagnosis: A Guide for Patients and Families (available in Spanish)

Distress in People with Cancer

Guide to Controlling Cancer Pain (available in Spanish)

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

Sexuality for the Man With Cancer (also available in Spanish)

Living With Uncertainty: The Fear of Cancer Recurrence

When Cancer Doesn’t Go Away

When Your Cancer Comes Back: Cancer Recurrence

Understanding cancer treatments

Understanding Radiation Therapy: A Guide for Patients and Families (also available in Spanish)

Understanding Cancer Surgery: A Guide for Patients and Families (also in Spanish)

Understanding Chemotherapy: A Guide for Patients and Families (also available in Spanish)

Clinical Trials: What You Need to Know

Managing Incontinence for Men With Cancer

Work, insurance, and finances

Health Insurance and Financial Assistance for the Cancer Patient

Returning to Work After Cancer Treatment

Working During Cancer Treatment

Family and caregiver concerns

Talking With Friends and Relatives About Your Cancer (also in Spanish)

What It Takes to Be a Caregiver

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

Helping Children When a Family Member Has Cancer: Dealing With Diagnosis (also available in Spanish)

When treatment is no longer working

Nearing the End of Life

Advance Directives

Hospice Care

Your American Cancer Society also has books that you might find helpful. Call us at 1-800-227-2345 or visit our bookstore online to find out about costs or to place an order.

National organizations and Web sites*

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

Urology Care Foundation
Toll-free number: 1-800-828-7866
Web site: www.urologyhealth.org

Offers free brochures on prostate cancer and screening as well as online information on diseases of the prostate, bladder, and other urology health issues in the “Urology A – Z” section of their website.

National Association for Continence
Toll-free number: 1-800-252-3337 (1-800-BLADDER)
Web site: www.nafc.org

This group offers information and support to all people who are living with incontinence and has information for men who have had prostate surgery. Also available in Spanish.

National Cancer Institute
Toll-free number: 1-800-422-6237 (1-800-4-CANCER); TYY: 1-800-332-8615
Web site: www.cancer.gov

Free, accurate, up-to-date information about cancer to patients, their families, and the general public; also helps people find clinical trials in their area

National Coalition for Cancer Survivorship
Toll-free number: 1-888-650-9127
1-877-622-7937 (1-877-NCCS-YES) for publications and Cancer Survivor Toolbox® orders
Web site: www.canceradvocacy.org

Offers information on work, health insurance, and more. The Cancer Survival Toolbox is a free, self-learning audio program to help cancer survivors and caregivers develop practical tools needed to deal with the diagnosis, treatment and challenges of cancer. Listen online or order CDs. Also in Spanish and Chinese.

Prostate Cancer Foundation (formerly "CaPCURE")
Toll-free number: 1-800-757-2873 (1-800-757-CURE) or 1-310-570-4700
Web site: www.pcf.org

You can find information on prostate cancer and treatment options as well as patient guides and survivor stories.

US Too International, Inc.
Toll-free number: 1-800-808-7866 (1-800-80-US-TOO)
Web site: www.ustoo.org

Free information about all stages of prostate cancer, different treatment options, new research findings and current clinical trials, and some referrals to local support groups

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

No matter who you are, we can help. Contact us anytime, day or night, for information and support. Call us at **1-800-227-2345** or visit www.cancer.org.

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