#### PROSTATE CANCER AWARENESS





#### WHAT IS PROSTATE 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 a 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 abnormal cells grow out of control.

Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. In most cases the cancer cells form a tumor. Cancer cells can also invade (grow into) other tissues, something that normal cells can't 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 is 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 abnormal cell does.

People can inherit damaged DNA, but most often the 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.

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 named (and treated) based on the place where it started. For example, prostate cancer that has spread to the bones is still prostate cancer, not bone cancer.

Different types of cancer can behave very differently. They grow at different rates and respond to different treatments. This 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 can't 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 rarely life threatening.

### **CAUSES, RISK FACTORS, AND PREVENTION**

## 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 affect a man's risk of getting it.

### 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 in Caribbean men of African ancestry than in men of other races. African-American men are also 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.

# Geography

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 when the cancer was found.

# **Gene changes**

Scientists have found several inherited gene changes that seem to raise prostate cancer risk, but they probably account for only a small percentage of cases overall. For example:

- Inherited mutations of the *BRCA1* or *BRCA2* genes raise the risk of breast and ovarian cancers in some families. Mutations in these genes may also increase prostate cancer risk in some men.
- Men with Lynch syndrome (also known as hereditary non-polyposis colorectal cancer, or HNPCC), a condition caused by inherited gene changes, have an increased risk for a number of cancers, including prostate cancer.

Other inherited gene changes can also raise a man's risk of prostate cancer. For more on some of these gene changes, see "<u>Do we know what causes prostate cancer?</u>"

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.

### 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 aren't 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. But 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 <u>obese</u> (very overweight) is linked with a higher overall risk of getting prostate cancer.

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 <u>smoking</u> and prostate cancer risk. Some research has linked smoking to a possible small increase in the risk of death from prostate cancer, but this finding 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 their risk of prostate cancer.

# 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, because they can lead to inflammation of the prostate. So far, studies have not agreed, and no firm conclusions have been reached.

## Vasectomy

Some studies have suggested that men who have had a vasectomy (minor surgery to make men infertile) have a slightly increased risk for prostate cancer. But other studies have not found an increased risk among men who have had this operation. Research on this possible link is still under way.

# **EARLY DETECTION, DIAGNOSIS, AND STAGING**

## Can prostate cancer be found early?

Screening refers to testing to find a disease such as cancer in people who don't 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 in more detail in our document <u>Prostate Cancer Prevention and Early Detection</u>.

If the results of either one of these tests are abnormal, <u>further testing</u> 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 <u>stage</u> than if no screening were done.

There is no question that screening can help find many prostate cancers early, but there are still questions about whether this saves lives. There are clearly both pros and cons to the prostate cancer screening tests in use today.

At this time, the American Cancer Society (ACS) recommends that men thinking about having 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 prostate cancer screening and treatment.

To learn more about prostate cancer screening and the current ACS screening guidelines, see our document *Prostate Cancer Prevention and Early Detection*.

#### TREATING PROSTATE CANCER

# 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 <u>diagnosed</u> and <u>staged</u>, you have a lot to think about before you and your doctor choose a treatment plan. You might feel that you must make a decision quickly, but it's important to give yourself time to absorb and process the information you have learned. Ask questions of your cancer care team. See the section "<u>What should you ask your doctor about prostate cancer?</u>" for a list of some questions to ask.

Depending on the situation, the treatment options for men with prostate cancer might 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 have
- The stage and grade of your cancer
- Your feelings (and your doctor's opinion) about the need to treat the cancer right away

\_

- The likelihood that each type of treatment will cure your cancer (or help in some other way)
- 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 they have several choices. Prostate cancer is a complex disease, and doctors can 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.

The main types of doctors who treat prostate cancer include:

- Urologists: surgeons who treat 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

Your primary care doctor can also be a helpful source of information as you sort through your treatment options. It's 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.

Many other specialists might be part of your treatment team as well, including physician assistants (PAs), nurse practitioners (NPs), 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 <u>Health Professionals Associated With Cancer Care</u>.

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
- Dealing with prostate cancer that remains or recurs after treatment

#### TALKING WITH YOUR DOCTOR

### What should you ask your doctor about prostate cancer?

It's 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 <u>tests</u> (if any) do you recommend, and why?
- Are there other types of doctors I should talk to before deciding on treatment?

- What is the <u>clinical stage and Gleason score (grade)</u> of my cancer? What do those mean to me? 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 <u>radical prostatectomy</u> or <u>radiation</u>? Why or why not?
- 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?
- What risks or side effects should I expect from my treatment options?
- 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 be like? Where will it be done?
- How would treatment affect my daily activities?
- What are the chances my cancer will come back with the treatment plans 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?

Along with 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 still might want to have children, ask if there is a possibility you could become impotent or sterile. You also might want to ask if you qualify for any clinical trials.

Keep in mind that doctors aren't the only ones who can give you information. Other health care professionals, such as nurses and social workers, may have the answers to some of your questions. You can find out more about speaking with your health care team in our document <u>Talking With Your Doctor</u>.

#### **AFTER TREATMENT**

# What happens after treatment for prostate cancer?

For most men with prostate cancer, treatment may can 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 accept this uncertainty and are living full lives. Our document *Living With Uncertainty: The Fear of Cancer Recurrence* talks more about this.

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

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

### Follow-up care

Even if you have completed treatment, your doctors will still want to watch you closely. It's 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 probably 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 might also be done, depending on your medical situation.

Almost any cancer treatment can have side effects. Some might 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 even many years after treatment, which is why it's 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's thought to be located and what types of <u>treatment</u> you've already had. For more information, see the section "<u>Prostate cancer that remains or recurs after treatment</u>." For more general information on dealing with a recurrence, you may also want to see our document <u>When Your Cancer Comes Back: Cancer Recurrence</u>.

## Seeing a new doctor

At some point after your treatment, you may be seeing a new doctor who doesn't know anything about your medical history. It's important to be able to give your new doctor the details of your diagnosis and treatment. Gathering this information soon after treatment may be easier than trying to get it at some point in the future. Make sure you have this information handy (and always keep copies for yourself):

- 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 <u>radiation therapy</u>, a copy of your treatment summary
- Copies of imaging tests (CT or MRI scans, etc.), which can usually be stored digitally (on a DVD, etc.)
- If you stayed in the hospital, a copy of the discharge summary that the doctor wrote when you were sent home

- If you had <u>hormone therapy</u>, <u>chemotherapy</u>, or other drug treatments, a list of your drugs, drug doses, and when you took them
- The names and contact information of the doctors who treated your cancer

It is also very important to keep 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.

#### WHAT'S NEW IN PROSTATE CANCER RESEARCH?

# 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 gene changes linked to prostate cancer is helping scientists better understand how prostate cancer develops. 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 might benefit from 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 some families. This mutation is rare, though, found in less than 2% of the men with prostate cancer that were studied.

The *HOXB13* gene mutation and most of the other gene mutations that have been studied so far as factors that might increase prostate cancer risk 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 <u>active surveillance</u>.

### 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. Some 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 in 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.

Some research has suggested that men who take aspirin daily for a long time might have a lower risk of getting and dying from prostate cancer, but more research is needed to confirm this.

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 are discussed in our document *Prostate Cancer Prevention and Early Detection*.

### 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 our document <u>Prostate Cancer Prevention and Early Detection</u>.

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. 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, Progensa, looks at the level of prostate cancer antigen 3 (PCA3) in the urine after a digital rectal exam (DRE). (The DRE pushes some of the prostate cells into the urine.) The higher the level, the more likely that prostate cancer is present. In studies, this test was used along with the PSA test.

Another test looks for an abnormal gene change called *TMPRSS2:ERG* in prostate cells in urine collected after a DRE. 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 see if this test can be used for early detection of prostate cancer.

### Diagnosis

Doctors doing prostate biopsies often rely on <u>transrectal ultrasound</u> (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. In this approach, the patient is first injected with a contrast agent containing microbubbles, which helps improve the ultrasound images. Promising results have been reported, but more studies will be needed before its use becomes common.

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 determining a man's treatment options. 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 is working. Studies of this technique are now in progress.

#### **Treatment**

Newer treatments are being developed, and improvements are being made among many standard prostate cancer treatment methods.

#### Surgery

Doctors are constantly improving the <u>surgical techniques</u> used to treat prostate cancer. The goal is to remove all of the cancer while lowering the risk of complications and side effects from the surgery.

# 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. Current methods such as conformal radiation therapy (CRT), intensity modulated radiation therapy (IMRT), and proton beam radiation help doctors avoid giving radiation to normal tissues as much as possible. These methods are expected to increase the effectiveness of radiation therapy while reducing the side effects.

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**

Some early research has found that in men with a rising PSA level after surgery or radiation therapy, drinking pomegranate juice or taking a pomegranate extract may slow the time it takes for the PSA level to double. Larger studies are now looking for possible effects of pomegranate juices and extracts on prostate cancer growth.

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 choose not to have treatment for their localized prostate cancer may be able to slow its growth with intensive lifestyle changes. The men in the study 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 taking 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 are described in the section "Hormone therapy for prostate cancer." Others are now being studied as well. 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 <u>chemotherapy</u> drugs can affect prostate cancer. Some, such as docetaxel (Taxotere) and cabazitaxel (Jevtana) have been shown to help men live longer.

Early results from a recent large study found that in men with metastatic prostate cancer, giving chemotherapy earlier in the course of the disease seemed to help them live longer. Those in the study who got docetaxel along with hormone therapy as their first treatment lived more than a year longer than men who got only hormone therapy as their first treatment. These results are encouraging, but this study was done before newer forms of hormone therapy (abiraterone and enzalutamide) became available, so it's not clear if the results would be the same today.

Other new chemo drugs and combinations of drugs are now being studied as well.

### **Immunotherapy**

The goal of immunotherapy is to boost the body's immune system to help fight off or destroy cancer cells.

#### **Vaccines**

Unlike vaccines against infections like measles or mumps, prostate cancer 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 (described in the section "Vaccine treatment for prostate cancer").

Several other types of vaccines to treat prostate cancer are being tested in <u>clinical trials</u>. One example is PROSTVAC, which 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, and a larger study is now under way.

# Immune checkpoint inhibitors

An important part of the immune system is its ability to keep itself from attacking other normal cells in the body. To do this, it uses "checkpoints" – molecules on immune cells that need to be turned on (or off) to start an immune response. Cancer cells sometimes use these checkpoints to avoid being attacked by the immune system. But newer drugs that target these checkpoints hold a lot of promise as cancer treatments.

For example, the drug ipilimumab (Yervoy) targets a checkpoint molecule called *CTLA-4* on certain immune cells. This drug is already used to treat advanced melanoma, and is now being tested in men with advanced prostate cancer. Early study results with this drug have shown some benefit, but a recent larger study didn't find it helped men live longer.

Other new drugs target immune checkpoints such as PD-1 or PDL-1. In some other cancers such as melanoma, these types of drugs have been shown to shrink a larger portion of tumors than ipilimumab. Studies are now being done to see how well they might work against prostate cancer.

One promising approach for the future might be to combine a checkpoint inhibitor with a prostate cancer vaccine. This might strengthen the immune response and help the vaccine to work better.

### **Targeted therapy drugs**

Newer drugs are being developed that work in different ways from standard chemo drugs. These drugs target specific parts of cancer cells or their surrounding environments. Each type of targeted therapy works differently, but all alter the way a cancer cell grows, divides, repairs itself, or interacts with other cells.

For example, drugs called *angiogenesis inhibitors* target the growth of new blood vessels (angiogenesis) that cancer cells need to grow. Cancers that stimulate many new vessels to grow are harder to treat and have a poorer outlook.

Several anti-angiogenic drugs have been tested in clinical trials. One of these is thalidomide (Thalomid<sup>®</sup>), which has been approved by the FDA to treat patients with multiple myeloma.

It was combined with chemotherapy in an early 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.

Several other angiogenesis inhibitors are now being tested as well.

### Treating cancer that has spread 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 is passed through the probe to heat and destroy 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.

Source

