

# **Treating Prostate Cancer**

If you've been diagnosed with prostate cancer, your cancer care team will discuss your treatment options with you. It's important to think about the benefits of each treatment option compared to the possible risks and side effects.

### How is prostate cancer treated?

Depending on each person's situation, treatment options for prostate cancer might include:

- Observation or Active Surveillance for Prostate Cancer
- Surgery for Prostate Cancer
- Radiation Therapy for Prostate Cancer
- Cryotherapy, HIFU, and Other Ablative Treatments for Prostate Cancer
- Hormone Therapy for Prostate Cancer
- Chemotherapy for Prostate Cancer
- Immunotherapy for Prostate Cancer
- Targeted Drug Therapy for Prostate Cancer
- Treatments for Prostate Cancer Spread to Bones

### **Common treatment approaches**

Treatments for prostate cancer are generally used one at a time, although in some cases they may be combined.

- Initial Treatment of Prostate Cancer, by Stage and Risk Group
- Following PSA Levels During and After Prostate Cancer Treatment
- Treating Prostate Cancer That Doesn't Go Away or Comes Back After Treatment

### Who treats prostate cancer?

The main types of doctors who treat prostate cancer include:

- **Urologist:** A surgeon who treats diseases of the urinary system and male reproductive system (including the prostate)
- Radiation oncologist: A doctor who treats cancer with radiation therapy
- **Medical oncologist:** A doctor who treats cancer with medicines, such as chemotherapy, hormone therapy, targeted therapy, and immunotherapy

Many other specialists may be involved in your care as well, including nurse practitioners (NPs), physician assistants (PAs), nurses, nutritionists, pharmacists, social workers, rehabilitation specialists, and other health professionals.

• Health Professionals Who Are Part of a Cancer Care Team

## Making treatment decisions

It's important to discuss all your treatment options, including their goals and possible side effects, with your doctors to help make the decision that best fits your needs. Some important things to consider include:

- The stage and grade of your cancer
- Your age and expected life span
- Any other serious health conditions you have
- Your feelings (and your doctor's opinion) about the need to treat the cancer right away
- The likelihood that treatment will cure your cancer (or help in some other way)
- Your feelings about the possible side effects from each treatment

You may feel that you must make a decision quickly, but it's important to give yourself time to absorb the information you have just learned. Ask questions if there is anything you're not sure about.

If time permits, it's often a good idea to seek a second opinion. A second opinion can give you more information and help you feel more confident about the treatment plan you choose.

Questions to Ask About Prostate Cancer

- Seeking a Second Opinion
- Considering Treatment Options for Early Prostate Cancer

## Thinking about taking part in a clinical trial

Clinical trials are carefully controlled research studies that are done to get a closer look at promising new treatments or procedures. Clinical trials are one way to get state-ofthe art cancer treatment. In some cases they may be the only way to get access to newer treatments. They are also the best way for doctors to learn better methods to treat cancer.

If you would like to learn more about clinical trials that might be right for you, start by asking your doctor if your clinic or hospital conducts clinical trials.

<u>Clinical Trials</u>

### Considering complementary, integrative, and alternative methods

You may hear about other methods to relieve symptoms or treat your cancer that your doctors haven't mentioned. They can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

**Complementary and integrative** methods are treatments that are used **along with** your regular medical care. **Alternative** treatments are used **instead of** standard medical treatment. Although some complementary and integrative methods might be helpful in relieving symptoms or helping you feel better, many have not been proven to work. Some might even be harmful.

Be sure to talk to your cancer care team about any method you are thinking about using. They can help you learn what is known (or not known) about the method, which can help you make an informed decision.

<u>Complementary and Integrative Medicine</u>

### Help getting through cancer treatment

People with cancer need support and information, no matter what stage of illness they may be in. Knowing all of your options and finding the resources you need will help you make informed decisions about your care.

Whether you are thinking about treatment, getting treatment, or not being treated at all, you can still get supportive care to help with pain or other symptoms. Communicating with your cancer care team is important so you understand your diagnosis, what treatment is recommended, and ways to maintain or improve your quality of life.

Different types of programs and support services may be helpful, and they can be an important part of your care. These might include nursing or social work services, financial aid, nutritional advice, rehab, or spiritual help.

The American Cancer Society also has programs and services - including rides to treatment, lodging, and more - to help you get through treatment. Call our Cancer Knowledge Hub at 1-800-227-2345 and speak with one of our caring, trained cancer helpline specialists. Or, if you prefer, you can use our chat feature on cancer.org to connect with one of our specialists.

- Palliative Care
- Programs & Services

## Choosing to stop treatment or choosing no treatment at all

For some people, when treatments have been tried and are no longer controlling the cancer, it could be time to weigh the benefits and risks of continuing to try new treatments. Whether or not you continue treatment, there are still things you can do to help maintain or improve your quality of life.

Some people, especially if the cancer is advanced, might not want to be treated at all. There are many reasons you might decide not to get cancer treatment, but it's important to talk to your doctors as you make that decision. Remember that even if you choose not to treat the cancer, you can still get supportive care to help with pain or other symptoms.

People who have advanced cancer and who are expected to live less than 6 months may want to consider hospice care. Hospice care is designed to provide the best possible quality of life for people who are near the end of life. You and your family are encouraged to talk with your doctor or a member of your supportive care team about hospice care options, which include hospice care at home, a special hospice center, or other health care locations. Nursing care and special equipment can make staying at home a workable option for many families.

- If Cancer Treatments Stop Working
- Hospice Care

The treatment information given here is not official policy of the American Cancer 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 your cancer care team any questions you may have about your treatment options.

# **Observation or Active Surveillance for Prostate Cancer**

Not all prostate cancers are the same. Some can grow quickly, but others tend to grow very slowly. Some men with slow-growing prostate cancers (especially men who are older or have other serious health problems) might never need treatment. Instead, their doctors may recommend **active surveillance** or **observation** (sometimes called **watchful waiting**).

- What are active surveillance and observation?
- When are these options used?
- Comparing active surveillance and treatment

## What are active surveillance and observation?

The terms active surveillance and observation mean something slightly different.

**Active surveillance** is often used to mean monitoring the cancer closely, with a plan to treat it if tests show it's starting to grow more quickly. Usually this approach includes doctor visits with a prostate-specific antigen (PSA) blood test about every 6 months and a digital rectal exam (DRE) about once a year. Prostate biopsies and imaging tests may be done every 1 to 3 years as well. Exactly how often <u>tests</u><sup>1</sup> are done can be tailored to some extent, based on each man's situation and preferences.

If your test results change, your doctor would then talk to you about treatment options to try to cure the cancer.

**Observation (watchful waiting)** is sometimes used to describe a less intense type of follow-up that includes fewer tests and that relies more on changes in a man's <u>symptoms</u><sup>2</sup> to decide if treatment is needed. This is more likely to be a good option for men who are older and/or have other serious health problems.

No matter which term your doctor uses, it's very important for you to understand exactly what they mean when they refer to it.

## When are these options used?

One of these approaches might be recommended (or at least be an option) if your cancer:

- Isn't causing any symptoms
- Is small and is just in the prostate
- Is expected to grow slowly, because it's in the very low, low, or favorable intermediate-**risk group**, and/or based on results from a **molecular test** of the cancer cells. To learn more, see <u>Risk Groups and Lab Tests to Help Determine</u> <u>Risk from Localized Prostate Cancer<sup>3</sup></u>.

These approaches are not likely to be good options if you have a fast-growing cancer or if the cancer is likely to spread outside the prostate.

The main advantage of active surveillance and observation is that these approaches allow some men with slow-growing cancers to avoid (or at least delay) treatments, such as surgery or radiation, which can often have bothersome side effects. Many of these men will never need treatment for their cancer. If they do eventually need treatment, it's unlikely that the wait will have had an effect on how long they live.

These approaches can have some potential downsides as well. For example, in a small percentage of cases, even a cancer that is thought to be slow growing might start growing faster or spread outside the prostate. This might be because the prostate biopsy missed a faster-growing part of the cancer, or because the cancer changed over time and became more aggressive. In either case, this might make it harder to cure the cancer than if it were treated when it was first found.

These approaches also require lifelong doctor visits and tests to monitor the cancer, especially with active surveillance. These visits and tests can be time-consuming, and waiting for test results might lead to anxiety for some men.

Finally, some men might just not be comfortable knowing they have "cancer" in their body, even if it's never likely to cause them any problems. This concern might lead some men to choose treatment, such as surgery or radiation therapy, even if the treatment is unlikely to help them live longer (and is still likely to cause side effects).

## Comparing active surveillance and treatment

Some men might want to know if studies have been done to compare active surveillance with immediate treatment with surgery or radiation therapy. Unfortunately, we don't have results from large studies directly comparing active surveillance with treatment in men with slow-growing prostate cancer.

Some studies have compared slightly different groups. For example, studies have compared observation (with less intense follow-up than active surveillance) versus treatment. Some studies that have looked at this issue also included men who would now be considered at higher risk (and therefore likely wouldn't be offered active surveillance today).

In the studies that have been done so far, it doesn't appear that men who are treated right away are likely to live any longer than men who choose active surveillance.

Finally, it's important to keep in mind that while there are still some questions about active surveillance, the tools doctors use to decide which men might benefit from it have improved a great deal in recent years. This includes the development of risk groups and molecular tests, as well as imaging tests, such as multiparametric MRI (mpMRI), all of which can help tell which men are most likely to be good candidates for active surveillance.

Doctors also continue to refine the best ways to monitor men who are on active surveillance, so they get the necessary tests to look for cancer progression while not being tested too often.

## **Hyperlinks**

- 1. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 2. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/signs-</u> <u>symptoms.html</u>
- 3. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/risk-groups.html</u>

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# **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 prostate gland.

- Radical prostatectomy
- Transurethral resection of the prostate (TURP)
- Orchiectomy (castration)
- More information about Surgery

Surgery is a common choice to try to cure prostate cancer if it is not thought to have spread outside the prostate gland.

## **Radical prostatectomy**

The main type of surgery for prostate cancer is a **radical prostatectomy**. In this operation, the surgeon (urologist) removes the entire prostate gland plus some of the tissue around it, including the <u>seminal vesicles</u><sup>1</sup>. Sometimes nearby lymph nodes are removed as well.

There are 2 main ways a surgeon can do a radical prostatectomy:

- In an **open prostatectomy**, the surgeon operates through a single long skin incision (cut) to remove the prostate and nearby tissues.
- In a laparoscopic prostatectomy, the surgeon makes several smaller incisions and uses long, thin surgical tools to remove the prostate and nearby tissues. Most often, the surgeon sits at a control panel to precisely move robotic arms that hold the tools (known as a robot-assisted prostatectomy or robotic prostatectomy). The operation can also be done with the surgeon holding the tools directly, although this is less common.

With either type of operation, if there's a reasonable chance the cancer might have spread to nearby <u>lymph nodes</u><sup>2</sup> (based on your <u>PSA level</u><sup>3</sup>, <u>prostate biopsy</u><sup>4</sup> results, and other factors), the surgeon may first remove some of these lymph nodes (known as a **pelvic lymph node dissection**). The nodes are sent to the lab to be looked at right away for cancer cells. If cancer cells are found in any of the nodes, the surgeon might not continue with the surgery. This is because it's unlikely that the cancer can be cured with surgery, and removing the prostate could lead to serious side effects.

### **Open prostatectomy**

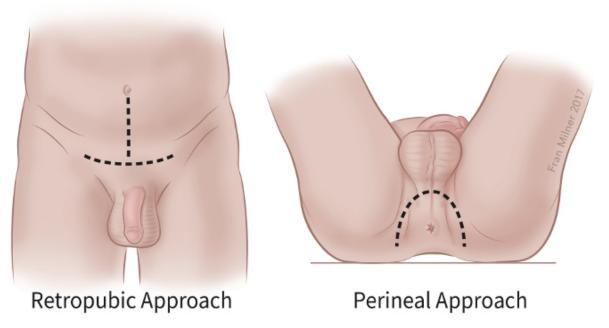
This type of surgery is done less often than in the past, as robotic prostatectomy (see below) has become more common. There are 2 main approaches for an open prostatectomy.

### Radical retropubic prostatectomy

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

After the prostate and nearby structures have been removed, and while you are still under anesthesia, a catheter (thin, flexible tube) will be put in your penis to help drain your bladder. The catheter will usually stay in place for 1 to 2 weeks while you heal. 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 your activities will be limited for several weeks.



## Radical perineal prostatectomy

In this open operation, the surgeon makes the cut (incision) in the skin between the anus and scrotum (the perineum), as shown in the picture above.

This approach is used less often because it's more likely to lead to erection problems and because the nearby lymph nodes can't be removed during the operation. But it is often a shorter operation, and it may result in less pain and an easier recovery than a retropubic prostatectomy.

This approach might be an option if you aren't concerned about erections and if you don't need lymph nodes removed. It also might be used if you have other medical conditions that might make retropubic surgery difficult for you. It is just as likely to cure prostate cancer as the retropubic approach if done correctly.

After the surgery, and 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 your activities will be limited for several weeks.

## Laparoscopic prostatectomy (including robotic prostatectomy)

Laparoscopic surgery is done through several small incisions in the abdomen, rather than one large incision. The surgeon inserts a **laparoscope**, which is a long, thin tube with a light and tiny video camera on the end, through one of the openings so they can see inside the body. Long, thin surgery instruments are then inserted through the other incisions to perform the operation.

This approach to prostatectomy (particularly robotic prostatectomy) has become much more common in recent years.

### Laparoscopic radical prostatectomy

For a laparoscopic radical prostatectomy (LRP), the surgeon holds the handles of the long instruments directly to maneuver them inside the belly and remove the prostate. This approach is not used as often as robotic prostatectomy.

### Robotic prostatectomy

This approach, also known as **robotic-assisted laparoscopic radical prostatectomy** or **robot-assisted prostatectomy**, is the most common way prostatectomy is done in the United States.

This operation is done using a robotic system. The surgeon sits at a control panel in the operating room and moves robotic arms to operate through several small incisions, usually in the patient's abdomen (although it can also be done with a perineal approach). The robotic system helps the surgeon move the instruments more precisely than if they were holding the laparoscopic tools directly in their hands.

## Robotic versus open radical prostatectomy: Things you should know

Robotic prostatectomy is the most common surgery to treat prostate cancer in the United States (and some other countries). That is largely because this operation has some short-term advantages over open radical prostatectomy. For example, it usually results in:

- Less blood loss during the operation
- Less pain after the operation
- A shorter hospital stay
- A quicker recovery time
- Less time the urinary catheter needs to stay in place
- A lower risk of some rare but potentially serious side effects

However, the results of robotic and open prostatectomy seem to be about the same when it comes to the long-term side effects that many men are most concerned about, including erection problems and trouble holding urine (incontinence). (These are described below.)

There also doesn't appear to be much difference between robotic and open prostatectomy when it comes to long-term outcomes. That is, studies haven't shown that either approach is clearly better than the other when it comes to how likely the cancer is to return after surgery or how likely a man is to die from prostate cancer. Both approaches generally result in good outcomes when done by experienced surgeons.

In some instances, there might be clear reasons to favor one approach over the other.

But no matter which prostatectomy approach you choose, the biggest factor in the success of your surgery is likely to be the experience and skill of your surgeon. Because of this, it's very important to find an experienced surgeon whom you're comfortable with and whom you can trust.

### **Risks of prostatectomy**

The risks with any type of radical prostatectomy are much like those of any major surgery. Problems during or shortly after the operation can include:

- Reactions to anesthesia
- Bleeding from the surgery
- Blood clots in the legs or lungs
- Damage to nearby organs
- Infections at the surgery site

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

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

Your risks depend, in part, on your overall health, your age, and the skill of your surgical team.

### Side effects of prostatectomy

The major possible side effects of radical prostatectomy are:

- Urinary incontinence (being unable to control urine)
- Erectile dysfunction (problems getting or keeping erections)

These side effects can also occur with some other forms of prostate cancer treatment.

Other side effects are also possible (see below).

### Urinary incontinence

You may not be able to control your urine, or you may have leakage or dribbling after your surgery. Being incontinent can affect you not only physically, but also emotionally and socially. These are the major types of incontinence:

• Men with **stress incontinence** might leak urine when they cough, laugh, sneeze, or exercise. Stress incontinence is the most common type after prostate surgery. It's usually caused by problems with the valve that keeps urine in the bladder (the

bladder sphincter). Prostate cancer treatments can damage this valve or the nerves that keep the valve working.

- Men with **overflow incontinence** have trouble emptying their bladder. 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 urinate. This happens 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, bladder control usually improves slowly over several weeks or months. But doctors can't predict for sure how any man will be affected. In general, older men tend to have more incontinence problems than younger men. Large cancer centers, where prostate surgery is done often and surgeons have a lot of experience, generally report fewer problems with incontinence.

Incontinence can be treated. Even if your incontinence can't be corrected completely, it can still be helped. To learn about managing and living with incontinence, see <u>Bladder</u> and <u>Bowel Incontinence</u><sup>5</sup>.

## Erectile dysfunction (impotence)

This means you can't get an erection sufficient for sexual penetration.

Erections are controlled by 2 tiny bundles of nerves that run along either side of the prostate. If you can have erections before surgery, the surgeon will try not to injure these nerves during the prostatectomy. This is known as a **nerve-sparing** approach. But if the cancer is growing into or very close to the nerves, the surgeon will need to remove them.

If both nerves are removed, you won't be able to have spontaneous erections, but you might still be able to have erections using some of the aids described below. If the nerves on only one side are removed, you might still have erections, but the chance is lower than if neither were removed. If neither nerve bundle is removed, you might have normal erections at some point after surgery.

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. Most men will probably have at least some loss of ability to have an erection, but the younger you are, the less

likely you are to be seriously affected.

Surgeons who do many prostatectomies tend to report lower rates of erection problems among their patients than those who do the surgery less often. A wide range of rates have been reported in the medical literature, but each man's situation is different, so the best way to get an idea of your chances for recovering erections is to ask about your doctor's success rates and what the outcome is likely to be in your case.

If your ability to have erections does return after surgery, it often returns slowly. In fact, it can take from a few months to 2 or more years. During the first few months, you will probably not be able to have a spontaneous erection, so you may need to use medicines or other treatments.

Many doctors feel that regaining potency is helped along by trying 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, although it's not clear if they work better if taken daily or just on an as-needed basis. Be sure to talk to your doctor about your situation.

There are several options for treating erectile dysfunction:

- Phosphodiesterase-5 (PDE5) inhibitors, such as sildenafil (Viagra), vardenafil (Levitra), tadalafil (Cialis), and avanafil (Stendra), are pills that can help with erections. These drugs won't work if both nerves that control erections have been damaged or removed. Common side effects of these drugs include headache, flushing (skin becoming red and feeling warm), upset stomach, light sensitivity, and runny or stuffy nose. Rarely, these drugs can cause vision problems, possibly even blindness. Some other drugs such as nitrates, which are used to treat heart disease, can cause problems if you are taking a PDE5 inhibitor, so be sure your doctor knows what medicines you take.
- 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 might have side effects, such as pain, dizziness, and prolonged erection, but they are not usually serious.
- Vacuum devices are another option to create an erection. These are clear, plastic tubes connected to pumps that are placed over the penis. The pump sucks the air out of the tube, which draws blood into the penis to produce an erection. After the device is removed, the erection is maintained by placing an elastic ring around the

base of the penis, which keeps the blood from draining out. The ring is then removed after sex.

• **Penile implants** might restore your ability to have erections if other methods don't help. An operation is needed to put them inside the penis. There are several types of penile implants, including those using silicone rods or inflatable devices.

For more on coping with erection problems and other sexuality issues, see <u>Sex and the</u> <u>Adult Male With Cancer.</u><sup>6</sup>

## Changes in orgasm

After surgery, the sensation of orgasm should still be pleasurable, but there is no ejaculation of semen – the orgasm is "dry." This is because the glands that made most of the fluid for semen (the seminal vesicles and prostate) were removed during the prostatectomy, and the pathways used by sperm (the vas deferens) were cut. In some men, orgasms might become less intense. Less often, men report pain with orgasm.

## Loss of fertility

During a radical prostatectomy, the surgeon cuts the vas deferens, which are the pathways between the testicles (where sperm are made) and the urethra (through which sperm leave the body). Your testicles will still make sperm, but they can't leave the body as a part of the ejaculate. This means that a man can no longer father a child the natural way.

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. To learn more, see <u>Male Fertility and Cancer</u><sup>7</sup>.

### Lymphedema

This is a rare but possible complication of removing many of the lymph nodes around the prostate. Lymph nodes normally provide a way for fluid to return to the heart from all areas of the body. When nodes are removed, fluid can 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. You can learn more on our <u>lymphedema</u><sup>8</sup> page.

### Change in penis length

A possible effect of surgery is a small decrease in penis length. This can result from 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 often used to treat men with non-cancerous enlargement of the prostate called **benign prostatic hyperplasia (BPH)**. But it is also sometimes used in men with advanced prostate cancer to help relieve symptoms, such as trouble urinating. (It is not used to try to cure the cancer.)

During this operation, the surgeon removes the inner part of the prostate gland that surrounds the urethra (the tube through which urine leaves the bladder). The skin is not cut with this surgery. An instrument called a **resectoscope** is passed through the tip of the penis and into the urethra to the level of the prostate. Once it's in place, either electricity is passed through a wire to heat it or a laser is used to cut or vaporize the tissue.

This operation is done with either spinal anesthesia (which numbs the lower half of your body) or general anesthesia (where you are in a deep sleep), and it usually takes about an hour.

After surgery, a catheter (thin, flexible tube) is inserted through the penis and 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 used.

## **Orchiectomy (castration)**

In this operation, the surgeon removes the testicles, where most of the androgens (male hormones) are made. Although this is a type of surgery, its main effect is as a form of

hormone therapy. To learn more about this operation, see Hormone Therapy for Prostate Cancer.

## More information about Surgery

For more general information about surgery as a treatment for cancer, see <u>Cancer</u> <u>Surgery</u><sup>9</sup>.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u><sup>10</sup>.

## Hyperlinks

- 1. www.cancer.org/cancer/types/prostate-cancer/about/what-is-prostate-cancer.html
- 2. <u>www.cancer.org/cancer/diagnosis-staging/lymph-nodes-and-cancer.html</u>
- 3. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 4. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 5. <u>www.cancer.org/cancer/managing-cancer/side-effects/stool-or-urine-</u> <u>changes/bladder-incontinence.html</u>
- 6. <u>www.cancer.org/cancer/managing-cancer/side-effects/fertility-and-sexual-side-effects/sexuality-for-men-with-cancer.html</u>
- 7. <u>www.cancer.org/cancer/managing-cancer/side-effects/fertility-and-sexual-side-effects/fertility-and-men-with-cancer.html</u>
- 8. www.cancer.org/cancer/managing-cancer/side-effects/swelling/lymphedema.html
- 9. www.cancer.org/cancer/managing-cancer/treatment-types/surgery.html
- 10. www.cancer.org/cancer/managing-cancer/side-effects.html

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# **Radiation Therapy for Prostate Cancer**

Radiation therapy uses high-energy rays or particles to kill cancer cells.

- When might radiation therapy be used?
- Types of radiation therapy
- External beam radiation therapy (EBRT)
- Brachytherapy (internal radiation therapy)
- Radiopharmaceuticals
- More information about radiation therapy

## When might radiation therapy be used?

Depending on the <u>stage</u><sup>1</sup> of the prostate cancer and other factors, radiation therapy might be used:

- As the first treatment for cancer that is still just in the prostate gland (especially if the cancer is in a lower <u>risk group</u><sup>2</sup>). Cure rates for men with these types of cancers are about the same as those for men treated with <u>radical prostatectomy</u>.
- As part of the first treatment (along with hormone therapy) for cancers that are still just in the prostate but are in higher-risk groups, or for cancers that have grown outside the prostate gland and into nearby tissues
- If surgery doesn't remove the cancer completely, or if it comes back (recurs) in the area of the prostate after surgery
- If the cancer is advanced (for example, if it has spread to the bones), to help keep it under control for as long as possible and to help prevent or relieve symptoms

## Types of radiation therapy

The main types of radiation therapy used for prostate cancer are:

- External beam radiation
- Brachytherapy (internal radiation)
- Radiopharmaceuticals (medicines containing radiation that are injected into the body)

## External beam radiation therapy (EBRT)

In <u>EBRT</u><sup>3</sup>, 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, to treat cancers that have grown outside the prostate, or to help relieve symptoms such as bone pain if the cancer has spread to a specific area of bone.

For most types of external radiation, treatments are given 5 days a week in an outpatient center, for at least several weeks. Many centers now give slightly higher doses of radiation over fewer treatments, which is known as **hypofractionated radiation**. This allows the treatment to be completed in a shorter amount of time, and it seems to be just as effective.

Each treatment is much like getting an x-ray, although the radiation dose is stronger. The treatment itself is painless and typically lasts only a few minutes, although the setup time — getting you into place for treatment — takes longer.

Modern EBRT techniques can focus the radiation more precisely on the tumor than was possible in the past. This lets doctors give higher doses of radiation to the tumor 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 them less likely to damage surrounding normal tissues and organs.

## Intensity modulated radiation therapy (IMRT)

IMRT, an advanced form of 3D-CRT therapy, is the most common type of external radiation therapy for prostate cancer. It uses a computer-driven machine that moves around the patient as it delivers radiation. Along with shaping the beams and aiming them at the prostate from several angles, the intensity (strength) of the beams can be adjusted to limit the doses of radiation reaching nearby normal tissues. This lets doctors deliver an even higher radiation dose to the cancer.

IMRT is often used along with **image-guided radiation therapy (IGRT)**, in which an imaging test is used to create pictures of the prostate just before giving each treatment. Because the prostate's position in the body can vary slightly from day to day, IGRT can help ensure the radiation is aimed more precisely, which might result in fewer side effects.

A variation of IMRT is called **volumetric modulated arc therapy (VMAT)**. It uses a machine that delivers radiation quickly as it rotates once around the body. This allows each treatment to be given in just a few minutes. Although this can be more convenient, it's not yet clear if it's more effective than standard IMRT.

## Stereotactic body radiation therapy (SBRT)

This technique, also known as **stereotactic ablative radiotherapy (SABR)**, uses advanced image-guided techniques to deliver large doses of radiation to a precise area, such as the prostate. Because there are large doses of radiation in each dose, the entire course of treatment is given in 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.

SBRT might be an option to treat some cancers that are just in the prostate. The main advantage of SBRT over IMRT in this setting is that the treatment takes much less time (days instead of weeks). However, some side effects might be worse with SBRT than with IMRT.

SBRT might also be used to treat cancer that has spread to a small number of spots in the bones.

### **MRI-guided radiation therapy**

This approach combines some features of IMRT, IGRT, and SBRT therapies into one. It is done with a machine known as an **MRI-linac**, which combines an MRI scanner with a linear accelerator (linac, the machine that delivers the radiation).

As with other types of IGRT, MRI pictures can be taken before each treatment, so the aim of the radiation can be adjusted to account for any change in the position of the prostate (and the tumor) since the last treatment.

MRI images can also be taken while the radiation is being given. If body functions (like breathing or digestion) cause the tumor to move out of the path of the radiation, the radiation stops until it is aimed correctly again. This can help reduce the amount of radiation to healthy tissues and organs around the tumor.

### Proton beam radiation therapy

Proton beam therapy focuses beams of protons instead of x-rays on the cancer.

Standard radiation therapy is given in the form of x-rays (photons), which release their energy both before and after they hit their target. However, 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 cancer while doing less damage to nearby normal tissues. Proton beam radiation can be aimed with techniques similar to those used for 3D-CRT and IMRT.

Although in theory proton beam therapy might be more effective than using x-rays, so far studies haven't shown if this is true.

Proton beam therapy isn't available everywhere. 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

Some of the side effects from EBRT are the same as those from surgery, while others are different.

**Bowel problems:** The prostate and rectum are very close to each other, so the rectum is often exposed to some radiation when treating the prostate. This can irritate the rectum and cause a condition called **radiation proctitis**. It can lead to <u>diarrhea</u><sup>4</sup>, sometimes with blood in the stool, and rectal leakage. Most of these problems tend to go away over time, but in rare cases normal bowel function does not return.

To help lessen bowel problems, you may be told to follow a special diet during radiation therapy to help limit bowel movement during treatment. Sometimes a balloon-like device or gel (known as a **spacer**) is put between the rectum and the prostate before treatment. Creating more space between them can lessen the amount of radiation that reaches the rectum.

**Urinary 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. Urinary problems usually improve over time, but in some men they might never go away.

Some men develop **urinary incontinence** after treatment, which means they can't control their urine or have leakage or dribbling. As described in the surgery section, there are different levels and types of incontinence. Overall, this side effect occurs less often with radiation therapy than after surgery. The risk is low at first, but it goes up each year for several years after treatment.

Rarely, the urethra (the tube that carries urine from the bladder out of the body) may become very narrow or even close off, which is known as a **urethral stricture**. This can affect your ability to urinate, and it might require further treatment to open it up again.

**Erectile dysfunction (impotence):** Some men will have problems getting or maintaining erections after external radiation therapy. These problems usually don't occur right after radiation therapy but instead develop slowly over time. This is different from surgery, where erection issues occur right away and may get better over time. But overall, the long-term risk of erection problems is about the same after radiation as it is after surgery.

As with surgery, the older you are, the more likely it is you will have problems with erections. Erection problems can often be helped by treatments such as those listed in the surgery section, including medicines.

For more about coping with erection problems and other sexuality issues, see <u>Sex and</u> the Adult Male With Cancer<sup>5</sup>.

**Feeling tired:** Radiation therapy can cause <u>fatigue</u><sup>6</sup> that might not go away until a few weeks or months after treatment stops.

**Lymphedema:** Lymph nodes normally provide a way for fluid to return to the heart from all areas of the body. If the lymph nodes around the prostate are damaged by radiation, fluid can 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. See <u>lymphedema</u><sup>7</sup> to learn more.

## **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 alone is generally used only in men with early-stage prostate cancer that is in a lower-risk group.
- Brachytherapy combined with external radiation is sometimes an option for men who have a higher risk of the cancer growing outside the prostate.

The use of brachytherapy is also limited by some 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 might not work

as well in men with large prostate glands because it might be harder to place the seeds into all of the needed locations. One way to get around this may be to get a few months of hormone therapy beforehand to shrink the prostate.

An <u>imaging test<sup>8</sup></u>, such as transrectal ultrasound, is typically used to help guide the placement of the radioactive pellets. Special computer programs calculate the exact dose of radiation needed.

There are 2 types of prostate brachytherapy. Both are done in an operating room. You will get either spinal anesthesia (where the lower half of your body is numbed) or general anesthesia (where you are in a deep sleep), and you might need to stay in the hospital overnight. Either brachytherapy treatment can be used alone or combined with external beam radiation (given at a lower dose than if used by itself).

## Permanent (low dose rate, or LDR) brachytherapy

This approach uses pellets (seeds) of radioactive material (such as iodine-125 or palladium-103), which are about the size and shape of a grain of rice. The pellets are placed inside thin, hollow needles, which are inserted through the skin in the area between the scrotum and anus and into the prostate. The needles are then removed, leaving the pellets in place. They give off low doses of radiation for weeks or months. Radiation from the seeds travels a very short distance, so the seeds can give off a large amount of radiation in a very small area. This limits the amount of damage to nearby healthy tissues.

Usually, around 100 seeds are placed, but this depends on the size of the prostate. Because the seeds are so small, they seldom cause discomfort, and are simply left in place after their radioactive material is used up.

You may also get external beam radiation along with brachytherapy, especially if there is a higher risk that your cancer has spread (or might spread) outside the prostate.

## Temporary (high-dose rate, or HDR) brachytherapy

This technique is done less often. It uses higher doses of radiation that are left in the prostate for a short time.

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. A radioactive substance, such as iridium-192 or cesium-137, is then placed in the catheters, usually for 5 to 15 minutes.

Generally, about 1 to 4 brief treatments are given over 2 days, and then the radioactive substance is removed each time. 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.

## Possible risks and side effects of brachytherapy

**Need for radiation precautions:** If you get **permanent (LDR) brachytherapy**, the seeds will give off small amounts of radiation for several weeks or months. 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. If you plan on traveling, you might want to get a doctor's note regarding your treatment, as low levels of radiation can sometimes be picked up by detection systems at airports.

There's also a small risk that some of the seeds might move (migrate). You may be asked to strain your urine for the first week or so to catch any seeds that might come out. You may be asked to take other precautions as well, such as wearing a condom during sex. Be sure to 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, the chances of this causing ill effects seems to be very small. Still, seeds are now often implanted in connected strands, which can lower the risk of them migrating.

These types of precautions aren't needed after HDR brachytherapy, because the source of the radiation doesn't stay in the body after treatment.

**Bowel problems:** The prostate and rectum are very close to each other, so the radiation from brachytherapy can sometimes irritate the rectum and cause a condition called **radiation proctitis**. Bowel problems, such as rectal pain, burning, and/or diarrhea (sometimes with bleeding), can occur, but serious long-term problems are uncommon.

**Urinary problems:** Severe urinary incontinence (trouble controlling urine) isn't common after brachytherapy, but some men have problems with frequent urination or other symptoms due to irritation of the urethra, the tube that drains urine from the bladder. This tends to be worse in the weeks after treatment and to get better over time. Rarely, the urethra may get very narrow or even close off (known as a **urethral stricture**) and need to be opened with a catheter or surgery.

Erection problems: Some men will have problems getting or maintaining erections

after brachytherapy. Some studies have suggested that rates of erectile dysfunction might be lower after brachytherapy, but other studies have found that the rates are about the same as with external beam radiation or surgery. As with external radiation (and unlike surgery), erection problems usually don't occur right after brachytherapy but instead develop slowly over time.

In general, the younger you are and the better your sexual function before treatment, the more likely you will be to regain function after treatment.

Erection problems can often be helped by treatments, such as those listed in the surgery section, including medicines. For more about coping with erection problems and other sexuality issues, see <u>Sex and the Adult Male With Cancer</u><sup>9</sup>.

## Radiopharmaceuticals

Radiopharmaceuticals are drugs that contain radioactive elements. They are injected into a vein and travel through the blood to reach cancer cells that have spread to other parts of the body. These drugs then give off radiation that kills the cancer cells. (The type of radiation they use travels only a short distance, which helps limit side effects.) Unlike other types of radiation, these drugs can reach cancer anywhere in the body.

## Radiopharmaceuticals that target PSMA

Prostate-specific membrane antigen (PSMA) is a protein that is often found in large amounts on prostate cancer cells.

**Lutetium Lu 177 vipivotide tetraxetan** (also known as <sup>177</sup>Lu-PSMA-617 or Pluvicto) is a radiopharmaceutical that attaches to PSMA, bringing radiation directly to the prostate cancer cells.

This drug can be used to treat prostate cancer that has spread and that has already been treated with hormone therapy and chemotherapy. The cancer cells must also have the PSMA protein. Your doctor will order a <u>PSMA PET scan<sup>10</sup></u> before you get this drug to make sure the cancer cells have PSMA.

This drug is given as an injection or infusion into a vein (IV), typically once every 6 weeks for up to 6 doses.

### **Possible side effects**

Some of the more common side effects of this drug include:

- Feeling tired
- Dry mouth
- Nausea
- Loss of appetite
- Constipation

This drug can lower blood cell counts:

- A low red blood cell count can cause tiredness, weakness, pale skin, or shortness of breath.
- A **low blood platelet count** can lead to bleeding or bruising more easily than normal, or bleeding that is hard to stop.
- A **low white blood cell count** can lead to an increased risk of infections, which might show as a fever, chills, sore throat, or mouth sores.

This drug might **damage the kidneys**. Your doctor or nurse will likely advise you to drink plenty of fluids and to urinate often before and after getting this drug, to help protect the kidneys. Tell your doctor or nurse if you start to pass less urine than is normal for you.

This drug contains **radiation** that might stay in your body for several days after treatment, so your health care team will advise you on ways to protect yourself and others. You will likely be advised to drink plenty of fluids and to urinate often to help flush any excess drug from your body and help protect your bladder. You might also be advised to avoid close contact with other people, especially children and pregnant women, for at least a few days after each treatment.

## Radiopharmaceuticals that target the bones

Some radiopharmaceuticals are designed to settle in the bones, where they can help treat prostate cancer that has spread there. Radiopharmaceuticals that treat prostate cancer spread to the bones include:

- Radium-223 (Xofigo)
- Strontium-89 (Metastron)
- Samarium-153 (Quadramet)

These drugs are discussed in more detail in Treatments for Prostate Cancer Spread to Bones.

## More information about radiation therapy

To learn more about how radiation is used to treat cancer, see <u>Radiation Therapy</u><sup>11</sup>.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u><sup>12</sup>.

## **Hyperlinks**

- 1. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-</u> staging/staging.html
- 2. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/risk-groups.html</u>
- 3. <u>www.cancer.org/cancer/managing-cancer/treatment-types/radiation/external-beam-radiation-therapy.html</u>
- 4. <u>www.cancer.org/cancer/managing-cancer/side-effects/stool-or-urine-changes/diarrhea.html</u>
- 5. <u>www.cancer.org/cancer/managing-cancer/side-effects/fertility-and-sexual-side-effects/sexuality-for-men-with-cancer.html</u>
- 6. <u>www.cancer.org/cancer/managing-cancer/side-effects/fatigue-weakness-sleep.html</u>
- 7. www.cancer.org/cancer/managing-cancer/side-effects/swelling/lymphedema.html
- 8. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 9. <u>www.cancer.org/cancer/managing-cancer/side-effects/fertility-and-sexual-side-effects/sexuality-for-men-with-cancer.html</u>
- 10. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 11. www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html
- 12. www.cancer.org/cancer/managing-cancer/side-effects.html

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# **Cryotherapy, HIFU, and Other Ablative Treatments for Prostate Cancer**

Ablative treatments use extreme heat or cold or other methods to destroy (ablate) prostate tissue, rather than removing it with surgery or treating it with radiation.

- Cryotherapy
- High-intensity focused ultrasound (HIFU)
- Other types of ablative therapies

Ablative therapies might be used to treat the whole prostate gland, or just to treat the part of the prostate where the cancer is thought to be (which is known as **focal therapy**).

The main advantage of focal therapy is that it is likely to have fewer side effects than treatments that affect the whole prostate, such as surgery or radiation. However, it can have some limitations as well. For example:

- It's not yet clear if focal treatments work as well in the long term (although if the cancer does come back, these treatments can often be repeated, or other treatments can be tried).
- Focal therapy might not be a good option if the tumor is very close to the urethra (the tube that carries urine out of the bladder, which passes through the prostate) or the rectum.
- Men who get focal therapy typically still need the same type of follow-up after

treatment as men who choose active surveillance.

Some types of ablative treatments, such as **cryotherapy** and **high-intensity focused ultrasound (HIFU)**, might be options to treat prostate cancer in certain situations, such as after radiation therapy. Some doctors now offer these as initial treatment options for early-stage prostate cancers that are at <u>low risk of growing and spreading</u><sup>1</sup>, especially in men who don't want surgery or radiation but aren't comfortable with just active surveillance. However, most expert groups don't recommend ablative therapies as the first treatment for prostate cancer, unless surgery and radiation aren't good options. This is mainly because there isn't enough long-term data to show that these treatments are as effective as surgery or radiation.

Other types of ablative treatments, such as **photodynamic therapy (PDT)** and **focal laser ablation (FLA)**, are still being studied for treating prostate cancer, and most doctors still consider them to be experimental at this time.

## Cryotherapy

Cryotherapy (also called **cryosurgery** or **cryoablation**) is the use of very cold temperatures to freeze and kill prostate cancer cells. Even though it is sometimes called cryosurgery, it's not actually a type of surgery.

Compared with surgery or radiation therapy, doctors know much less about the longterm effectiveness of cryotherapy. While some forms of cryotherapy have been around for decades, modern cryotherapy techniques are still fairly new, so less is known about them.

## When is cryotherapy used?

Cryotherapy is sometimes used if the cancer has come back after radiation therapy.

It may be an option to treat men with low-risk, early-stage prostate cancer who can't have surgery or radiation therapy. However, most doctors don't use cryotherapy as the first treatment for prostate cancer.

As with brachytherapy, this may not be a good option for men with large prostate glands.

### How is cryotherapy done?

This procedure can be done with spinal or epidural anesthesia (where the lower half of your body is numbed) or general anesthesia (where you are in a deep sleep).

The doctor uses <u>transrectal ultrasound (TRUS)</u><sup>2</sup> to guide several thin, hollow probes (needles) through the skin between the anus and scrotum and into the prostate. Very cold gases are then passed through the needles to create an ice ball that freezes and destroys the prostate tissue. Warmer gases are then passed through the probes to thaw out the area. This process is usually repeated.

To be sure the prostate tissue is destroyed without too much damage to nearby structures, tiny probes are put in and around the prostate before the procedure to monitor the temperature. The doctor also carefully watches the ultrasound during the procedure to make sure the right areas are being treated. Warm saltwater is passed through a catheter in the urethra to keep it from freezing. The catheter is left in place for several weeks afterward to allow the bladder to empty while you recover.

After the procedure, you might need to stay in the hospital overnight, but many men can go home the same day.

Cryotherapy is less invasive than surgery, so there is usually less blood loss, a shorter hospital stay, a shorter recovery period, and less pain.

### Possible side effects of cryotherapy

Side effects from cryotherapy depend on how much of the prostate is treated. They tend to be worse if it is done in men who have already had radiation therapy, compared to men who have it as their first treatment.

Most men have <u>blood in their urine</u><sup>3</sup> 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.

Freezing might also affect the bladder and rectum, 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 often damages the nerves near the prostate that control erections. **Erectile dysfunction** is more common after cryotherapy than after radical prostatectomy. For information on coping with erection problems and other sexuality issues, see <u>Sex and</u> the Adult Male With Cancer<sup>4</sup>.

<u>Urinary incontinence<sup>5</sup></u> (having problems controlling urine) is rare in men who have

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

A very small percentage of men develop a **fistula** (an abnormal connection) between the rectum and bladder after cryotherapy. This rare but serious problem can allow urine to leak into the rectum, and it often requires surgery to repair.

## High-intensity focused ultrasound (HIFU)

HIFU uses highly focused ultrasound beams to heat and destroy prostate tissue. This treatment is still fairly new in the United States, although it's been used in some other countries for many years.

While HIFU devices have been approved by the US Food and Drug Administration (FDA) to destroy prostate tissue (and therefore doctors can use them to treat prostate cancer), these devices have not been approved specifically to treat prostate cancer. It's not yet clear how the long-term effectiveness of HIFU compares to surgery or radiation therapy.

## When is HIFU used?

HIFU might be a treatment option if prostate cancer has come back after radiation therapy.

Some doctors now offer HIFU as the first treatment for early-stage prostate cancers that are at low risk of growing and spreading. However, most expert groups in the United States don't recommend HIFU as a first-line treatment for prostate cancer at this time.

## How is HIFU done?

This procedure can be done with either spinal anesthesia (where the lower half of your body is numbed) or general anesthesia (where you are in a deep sleep).

A special ultrasound probe is inserted into the rectum, and it's first used to create 3D images of the prostate. These can be fused with images from other tests such as MRI, which can help the doctor determine which areas of the prostate need to be treated. The probe is then used to create focused, high-intensity ultrasound beams that precisely heat and destroy those areas of the prostate. The procedure typically takes 1 to 4 hours.

After the procedure, you'll have a urinary catheter, which will stay in place for up to a

week. Most men can go home the same day.

## Possible side effects of HIFU

Side effects after treatment can include:

- Pain in the treatment area
- Blood in the urine
- An increased risk of a urinary tract infection (UTI)
- Having trouble urinating
- Feeling the need to urinate often

The risks of long-term problems, such as urinary incontinence and erectile dysfunction, are likely to be lower than they are with treatments such as surgery or radiation therapy, although they are still possible.

## Other types of ablative therapies

Other types of ablative treatments are being developed as well. Some of these are now available, although most expert groups believe they need to be studied further before they become commonly used. Examples include:

**Transurethral ultrasound ablation (TULSA):** This procedure is similar to HIFU (described above) in that it uses high-intensity ultrasound beams to precisely heat and destroy parts or all of the prostate. But for TULSA, a thinner ultrasound probe is inserted through the tip of the penis and into the urethra (which runs through the prostate), rather than being inserted into the rectum. Real-time MRI is then used to image the prostate and guide treatment.

**Focal laser ablation (FLA):** In this approach, a thin laser fiber is inserted into the prostate near the tumor. This is typically done using MRI images for guidance, although some researchers are now studying the use of ultrasound as well. The laser is then activated to heat and destroy the prostate tissue.

**Photodynamic therapy (PDT):** For PDT, a light-activated drug is injected into the blood through an IV. A short time later, a low-energy laser light source is inserted into the prostate and directed at the tumor using thin optical fibers. The light activates the drug, which then destroys the blood vessels around the tumor. This procedure, which is also known as **vascular-targeted photodynamic therapy (VTP)**, is not yet available in the United States. To learn more about PDT in general, see <u>Getting Photodynamic</u>

## Therapy<sup>6</sup>.

**Irreversible electroporation (IRE):** For this treatment, long needles (electrodes) are place around the tumor to create a strong electrical field within the tumor. This causes holes (pores) to form in the walls of the cancer cells, leading to their death. This approach doesn't use heat or cold to destroy the cells, so it might prove useful in areas where it's important to protect vital structures like nearby blood vessels.

## **Hyperlinks**

- 1. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/risk-groups.html</u>
- 2. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 3. www.cancer.org/cancer/managing-cancer/side-effects/stool-or-urine-changes.html
- 4. <u>www.cancer.org/cancer/managing-cancer/side-effects/fertility-and-sexual-side-effects/sexuality-for-men-with-cancer.html</u>
- 5. <u>www.cancer.org/cancer/managing-cancer/side-effects/stool-or-urine-</u> <u>changes/bladder-incontinence.html</u>
- 6. <u>www.cancer.org/cancer/managing-cancer/treatment-types/radiation/photodynamic-therapy.html</u>

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# **Hormone Therapy for Prostate Cancer**

Hormone therapy is also called **androgen deprivation therapy (ADT).** The goal of this treatment is to reduce levels of male hormones, called androgens, in the body, or to stop them from fueling prostate cancer cell growth. Several types of hormone therapy can be used to treat prostate cancer.

- How does hormone therapy work?
- When is hormone therapy used?
- Treatment to lower testicular androgen levels
- Treatment to lower androgen levels from other parts of the body
- Drugs that stop androgens from working
- Current issues in hormone therapy
- More information about hormone therapy

#### How does hormone therapy work?

Androgens help prostate cancer cells grow. The main androgens in the body are testosterone and dihydrotestosterone (DHT). Most androgens are made by the testicles, but the adrenal glands (glands that sit above your kidneys), as well as the prostate cancer cells themselves, can also make androgens.

Lowering androgen levels or stopping them from getting into prostate cancer cells can often make prostate cancers shrink or grow more slowly for a time. But hormone therapy alone doesn't cure prostate cancer, and many cancers become resistant to hormone therapy over time.

### When is hormone therapy used?

Hormone therapy may be used:

- Along with radiation therapy as the first treatment for cancer that's still in or around the prostate, if the cancer is at <u>higher risk</u><sup>1</sup> for coming back after treatment
- Before radiation, to try to shrink the cancer to make treatment more effective
- If the cancer remains or comes back after treatment with surgery or radiation therapy (especially if the cancer has spread, or if it's not exactly clear where it is in the body)
- If the cancer has spread too far to be cured by surgery or radiation, or if you can't have these treatments for some other reason.

To learn more, see Initial Treatment of Prostate Cancer, by Stage and Risk Group and Treating Prostate Cancer That Doesn't Go Away or Comes Back After Treatment.

# Treatment to lower testicular androgen levels

Some hormone treatments use surgery or medicines to lower the levels of androgens made by the testicles.

#### **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 (such as testosterone and DHT) are made. This causes most prostate cancers to stop growing or shrink for a time.

This is done as an outpatient procedure. It is probably the least expensive and simplest form of hormone therapy. But unlike some of the other treatments, it is permanent, and many men have trouble accepting the removal of their testicles. Because of this, they may instead choose treatment with drugs that lower hormone levels (such as an LHRH agonist or antagonist – see below).

Some men having this surgery are concerned about how it will look afterward. If wanted, artificial testicles that look much like normal ones can be placed in the scrotum.

#### LHRH agonists

Luteinizing hormone-releasing hormone (LHRH) agonists (also called LHRH analogs or GnRH agonists) are drugs that lower the amount of testosterone made by the testicles. Treatment with these drugs is sometimes called **medical castration** because they lower androgen levels just as well as orchiectomy.

With these drugs, the testicles stay in place, but they will shrink over time, and they may even become too small to feel.

LHRH agonists 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 every 6 months. The LHRH agonists available in the United States include:

- Leuprolide (Lupron, Eligard) and leuprolide mesylate (Camcevi)
- Goserelin (Zoladex)
- Triptorelin (Trelstar)

When LHRH agonists are first given, testosterone levels go up briefly before falling to very low levels. This effect, called **tumor flare**, results from the complex way in which these drugs work. Some men whose cancer has spread to the bones may have bone pain. Men whose prostate has not been removed may have trouble urinating. If the cancer has spread to the spine, a short-term increase in tumor growth as a result of the flare could, in very rare cases, press on the spinal cord and cause pain or paralysis.

A flare can be avoided by giving drugs called **anti-androgens** (discussed below) for a few weeks when starting treatment with LHRH agonists.

#### LHRH antagonists

LHRH antagonists can be used to treat advanced prostate cancer. These drugs work in a slightly different way from the LHRH agonists, but they lower testosterone levels more quickly and don't cause tumor flare like the LHRH agonists do. Treatment with these drugs can also be considered a form of medical castration.

• **Degarelix (Firmagon)** is given as a monthly injection under the skin. Some men may notice problems at the injection site (pain, redness, and swelling).

• **Relugolix (Orgovyx)** is taken as pills, once a day, so it might allow for less frequent office visits.

#### **Possible side effects**

Orchiectomy and LHRH agonists and antagonists can all cause similar side effects from lower levels of hormones such as testosterone. These can include:

- Reduced or absent sexual desire
- Erectile dysfunction (impotence)
- Shrinkage of testicles and penis
- Hot flashes, which may get better or go away with time
- Breast tenderness and growth of breast tissue (gynecomastia)
- 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 levels
- Depression or mood swings

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.

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 this is not effective once breast enlargement has occurred.
- Several drugs can help prevent and treat osteoporosis.
- Depression can be treated with 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 thinking, concentrating, and/or with memory, but this has not been studied thoroughly. These problems are rarely severe, and most often affect only some types of memory. More studies are being done to look at this issue.

### Treatment to lower androgen levels from other parts of the body

LHRH agonists and antagonists can stop the testicles from making androgens, but cells in other parts of the body, such as the adrenal glands and prostate cancer cells themselves, can still make male hormones, which can fuel cancer growth. Some drugs can block the formation of androgens made by these cells.

**Abiraterone (Zytiga)** blocks an enzyme called CYP17, which helps stop cells in the body from making androgens.

Abiraterone can be used in men with advanced prostate cancer that is either:

- High risk (cancer with a high <u>Gleason score</u><sup>2</sup>, spread to several spots in the bones, or spread to other organs)
- Castration-resistant (cancer that is still growing despite low testosterone levels from an LHRH agonist, LHRH antagonist, or orchiectomy)

This drug is taken as pills every day.

Abiraterone doesn't stop the testicles from making testosterone, so men who haven't had an orchiectomy need to continue treatment with an LHRH agonist or antagonist. Because abiraterone also lowers the level of some other hormones in the body, a low dose of prednisone (a corticosteroid drug) needs to be taken during treatment as well to avoid certain side effects.

**Ketoconazole (Nizoral)**, first used for treating fungal infections, also blocks production of androgens made in the adrenal glands, much like abiraterone. It's 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 working.

Ketoconazole also can block the production of cortisol, an important steroid hormone in the body, so men treated with this drug often need to take a corticosteroid (such as prednisone or hydrocortisone).

Possible side effects: Abiraterone can cause joint or muscle pain, high blood

pressure, fluid buildup in the body, hot flashes, upset stomach, and diarrhea. Ketoconazole can cause elevated liver blood tests, nausea, vomiting, gynecomastia (enlargement of breast tissue in men), and skin rash.

# Drugs that stop androgens from working

For most prostate cancer cells to grow, androgens have to attach to a protein in the prostate cancer cell called an **androgen receptor**.

**Anti-androgens**, also called **androgen receptor antagonists**, are drugs that connect to androgen receptors, which stops the androgens from fueling tumor growth.

#### First-generation anti-androgens

These drugs were the first anti-androgens to become available, and they are often still used. Drugs of this type include:

- Flutamide (Eulexin)
- Bicalutamide (Casodex)
- Nilutamide (Nilandron)

These drugs are taken daily as pills.

In the United States, anti-androgens are most often used along with treatments that lower testosterone levels:

- An anti-androgen may be added to treatment if orchiectomy or an LHRH agonist or antagonist is no longer working by itself.
- An anti-androgen is also sometimes given for a few weeks when an LHRH agonist is first started. This can help prevent a tumor flare.
- An anti-androgen can also be combined with orchiectomy or an LHRH agonist as first-line hormone therapy. This is called **combined androgen blockade** (CAB).

In some men, if an anti-androgen is no longer working, simply stopping the antiandrogen can cause the cancer to stop growing for a short time. This is called the **antiandrogen withdrawal effect**, although it is not clear why it happens.

**Possible side effects:** Anti-androgens have similar side effects to LHRH agonists, LHRH antagonists, and orchiectomy. When these drugs are used alone, they may have

fewer sexual side effects. Sexual desire and erections 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.

#### Newer (second-generation) anti-androgens

Enzalutamide (Xtandi), apalutamide (Erleada), and darolutamide (Nubeqa) are newer types of anti-androgens. They can sometimes be helpful even when older antiandrogens are not.

- Any of these drugs can be helpful in men with cancer that has not spread but is no longer responding to other forms of hormone therapy (known as **non-metastatic** castration-resistant prostate cancer (nmCRPC)).
- Any of these drugs can also be used for metastatic castration-sensitive prostate cancer (mCSPC) (cancer that has spread but that is still responding to other forms of hormone therapy).
- Enzalutamide can also be used for non-metastatic castration-sensitive prostate cancer (nmCSPC) that appears to have come back after treatment based on a high PSA level (a biochemical recurrence), and that is thought to be at high risk for spreading to other parts of the body.
- Enzalutamide can also be used for metastatic castration-resistant prostate cancer (mCRPC).

These drugs are taken as pills each day.

**Side effects** can include diarrhea, fatigue, rash, and worsening of hot flashes. These drugs can also cause some nervous system side effects, including dizziness and, rarely, seizures. Men taking one of these drugs are more likely to fall, which may lead to injuries. Some men have also had heart problems when taking these newer types of anti-androgens.

#### Other androgen-suppressing drugs

**Estrogens** (female hormones) were once the main alternative to removing the testicles (orchiectomy) for men with advanced prostate cancer. Because of their possible side effects (including blood clots and breast enlargement), estrogens have been replaced by other types of hormone therapy. Rarely, estrogens may be tried if other hormone treatments are no longer working.

# 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 observation or active surveillance in men with early-stage prostate cancer who do not want surgery or radiation. Studies have not found that these men live any longer than those who don't get any treatment 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 levels are rising after surgery or radiation or men with advanced prostate cancer who don't yet have symptoms, it's not always clear when it is best to start hormone treatment.

Some doctors think that hormone therapy works better if it's started as soon as possible, even if a man feels well and isn't having any symptoms. Some studies have suggested that hormone treatment may slow the disease down and perhaps even help men live longer.

But not all doctors agree with this approach. Some are waiting for more evidence of benefit. They feel that because of the side effects of hormone therapy and the chance that the cancer could become resistant to therapy sooner, treatment shouldn't be started until a man has symptoms from the cancer. This issue is being studied.

#### Intermittent versus continuous hormone therapy

Some doctors believe that constant androgen suppression might not be needed, so they advise intermittent (on-again, off-again) treatment. This can allow for a break from side effects like decreased energy, sexual problems, and hot flashes.

In one form of intermittent hormone therapy, 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 how this approach compares to continuous hormone therapy. Some studies have found that continuous therapy might help men live longer, but other studies have not found such a difference.

#### Combined androgen blockade (CAB)

Some doctors advise androgen deprivation (orchiectomy or an LHRH agonist or antagonist) plus an anti-androgen for initial hormone therapy for advanced prostate cancer. Studies have suggested this may be more helpful than androgen deprivation alone.

#### Triple androgen blockade (TAB)

Some doctors have suggested taking combined therapy one step further, by adding a drug called a 5-alpha reductase inhibitor – either finasteride (Proscar) 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.

# Castration-sensitive, castration-resistant, and hormone-refractory prostate cancer

These terms are sometimes used to describe how well a man's prostate cancer is responding to hormone therapy.

- Castration-sensitive prostate cancer (CSPC), also known as hormonesensitive prostate cancer (HSPC), means the cancer is being controlled by keeping the testosterone level as low as what would be expected if the testicles were removed by castration. Levels can be kept this low with an orchiectomy, or by taking an LHRH agonist or an LHRH antagonist.
- **Castration-resistant prostate cancer (CRPC)** means the cancer is still growing even when the testosterone levels are at or below the level that would be expected with castration. Some of these cancers might still be helped by other forms of hormone therapy, such as abiraterone or one of the newer anti-androgens.
- Hormone-refractory prostate cancer (HRPC) refers to prostate cancer that is no longer helped by any type of hormone therapy, including the newer medicines.

# More information about hormone therapy

To learn more about how hormone therapy is used to treat cancer, see <u>Hormone</u>

Therapy<sup>3</sup>.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u><sup>4</sup>.

# **Hyperlinks**

- 1. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/risk-groups.html</u>
- 2. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 3. www.cancer.org/cancer/managing-cancer/treatment-types/hormone-therapy.html
- 4. www.cancer.org/cancer/managing-cancer/side-effects.html

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# **Chemotherapy for Prostate Cancer**

Chemotherapy (chemo) uses anti-cancer drugs injected into a vein or taken by mouth to reach cancer cells in most parts of the body.

- When is chemotherapy used?
- Chemo drugs used to treat prostate cancer
- How is chemotherapy given?
- Possible side effects of chemotherapy
- More information about chemotherapy

#### When is chemotherapy used?

Chemo isn't part of the treatment for most men with prostate cancer, but it can be used to treat advanced prostate cancer, especially if there is a lot of cancer outside the prostate gland. It can be used along with hormone therapy, or by itself if hormone

therapy is no longer working.

Chemo is not a standard treatment for early prostate cancer.

#### Chemo drugs used to treat prostate cancer

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

- Docetaxel
- Cabazitaxel
- Mitoxantrone
- Estramustine
- Carboplatin

Most often, docetaxel is the first chemo drug given. It is typically combined with a steroid drug, such as prednisone or dexamethasone. If docetaxel doesn't work (or stops working), cabazitaxel is often the next chemo drug tried (along with a steroid), although there may be other treatment options as well.

Docetaxel and cabazitaxel have been shown to help men live longer, on average, than older chemo drugs. They may shrink the cancer or slow its growth, and they may also reduce <u>symptoms</u><sup>1</sup>, resulting in a better quality of life. Still, chemo is very unlikely to cure prostate cancer.

Other chemo drugs are being studied for use in prostate cancer treatment as well.

#### How is chemotherapy given?

Chemo drugs for prostate cancer are typically given into a vein (IV) as an infusion over a certain period of time. This can be done in a doctor's office, chemotherapy clinic, or in a hospital setting. Some drugs, such as estramustine, are given as a pill.

Sometimes, a slightly larger and sturdier IV might be put into a vein to give chemo. These are known as <u>central venous catheters</u><sup>2</sup> (CVCs), central venous access devices (CVADs), or central lines. They are used to put medicines, blood products, nutrients, or fluids right into your blood. They can also be used to take out blood for testing. Many kinds of CVCs are available. The most common types are the port and the PICC line.

Doctors give chemo in cycles, with each period of treatment followed by a rest period to

give you time to recover from the effects of the drugs. Cycles are most often about 3 weeks long. The schedule varies depending on the drugs used. For example, with some drugs, the chemo is given only on the first day of the cycle. With others, it is given for a few days in a row, or once a week. Then, at the end of the cycle, the chemo schedule repeats to start the next cycle.

How long you'll get chemo depends on how well it's working and what side effects you have.

# 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 (where new blood cells are made), the lining of the mouth and intestines, and the hair follicles, also divide quickly. These cells can also be affected by chemo, which can lead to side effects.

The side effects of chemo depend on the type and dose of drugs given and how long they are taken. Some common side effects can include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Diarrhea
- Increased chance of infections (from having too few white blood cells)
- Easy bruising or bleeding (from having too few blood platelets)
- Fatigue (from having too few red blood cells)

These side effects usually go away once treatment is finished. There are often ways to lessen these side effects. For example, drugs can be given to prevent or reduce nausea and vomiting.

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

• **Docetaxel** and **cabazitaxel** sometimes cause severe allergic reactions. Medicines are given before each treatment to help prevent this. These drugs can also damage nerves (known as peripheral neuropathy), which can cause numbness, tingling, or burning sensations in the hands or feet.

- **Mitoxantrone** can, very rarely, cause <u>leukemia<sup>3</sup></u> several years later.
- Estramustine carries an increased risk of blood clots.

If you notice any side effects while getting chemo, report them to your cancer care team so that they can be treated promptly. In some cases, the doses of the chemo drugs may need to be reduced, or treatment may need to be delayed or stopped to prevent the effects from getting worse.

#### More information about chemotherapy

For more general information about how chemotherapy is used to treat cancer, see <u>Chemotherapy</u><sup>4</sup>.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u><sup>5</sup>.

# Hyperlinks

- 1. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/signs-</u> <u>symptoms.html</u>
- 2. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/tubes-lines-ports-catheters.html</u>
- 3. <u>www.cancer.org/cancer/survivorship/long-term-health-concerns/second-cancers-in-adults.html</u>
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# **Immunotherapy for Prostate Cancer**

Immunotherapy is the use of medicines to stimulate a person's own immune system to recognize and destroy cancer cells more effectively. Certain types of immunotherapy can be used to treat prostate cancer.

- Cancer vaccine
- Immune checkpoint inhibitors
- More information about immunotherapy

#### **Cancer vaccine**

**SipuleuceI-T (Provenge)** is a <u>cancer vaccine</u><sup>1</sup>. Unlike traditional vaccines, which boost the body's immune system to help prevent infections, this vaccine boosts the immune system to help it attack prostate cancer cells.

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

This vaccine is made specifically for each man. To make it, white blood cells (cells of the immune system) are removed from your blood over a few hours while you are hooked up to a special machine.

The cells are then sent to a lab, where they are mixed with a protein from prostate cancer cells called **prostatic acid phosphatase (PAP)**. The white blood cells are then sent back to the doctor's office or hospital, where they are given back to you by infusion into a vein (IV).

This process is repeated 2 more times, 2 weeks apart, so that you get 3 doses of cells. The cells help your other immune system cells attack the prostate cancer.

The vaccine hasn't been shown to stop prostate cancer from growing, but studies suggest it may help men live an average of several months longer. As with hormone therapy and chemotherapy, this type of treatment has not been shown to cure prostate cancer.

#### Possible side effects of vaccine treatment

Common side effects from the vaccine 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 couple of days. A few men may have more severe symptoms, including problems breathing and high blood pressure, which usually get better after treatment.

#### Immune checkpoint inhibitors

An important part of the immune system is its ability to keep itself from attacking the body's normal cells. To do this, it uses "checkpoint" proteins on immune cells, which act like switches that need to be turned on (or off) to start an immune response. Cancer cells sometimes use these checkpoints to keep the immune system from attacking them. But drugs that target these checkpoints, known as **checkpoint inhibitors**, hold a lot of promise as cancer treatments.

For example, **pembrolizumab (Keytruda)** and **dostarlimab (Jemperli)** are drugs that target PD-1, a checkpoint protein on immune system cells called T cells. By blocking PD-1, these drugs boost the immune response.

One of these drugs might be an option to treat some advanced prostate cancers, although this is rare.

**Pembrolizumab** can be used if the cancer cells have any of the following:

- A high level of microsatellite instability (MSI-H) or a defect in a mismatch repair gene (dMMR)
- A high tumor mutational burden (TMB-H), meaning the cancer cells have many gene mutations

**Dostarlimab** can be used if the cancer cells have a **defect in a mismatch repair gene** (dMMR).

Unfortunately, these types of changes aren't common in prostate cancer. But for men whose cancer cells have one of these changes, one of these drugs might be helpful.

These drugs are given as an intravenous (IV) infusion, typically every 3 to 6 weeks.

Doctors are also studying these and other checkpoint inhibitors combined with other types of medicines in treating prostate cancer.

#### Possible side effects

Side effects of these drugs can include fatigue, cough, nausea, itching, skin rash, decreased appetite, constipation, joint pain, and diarrhea.

Other, more serious side effects occur less often.

**Infusion reactions:** Some people might have an infusion reaction while getting one of these drugs. This is like an allergic reaction, and can include fever, chills, flushing of the face, rash, itchy skin, feeling dizzy, wheezing, and trouble breathing. It's important to tell your doctor or nurse right away if you have any of these symptoms while getting this drug.

**Autoimmune reactions:** These drugs work by basically removing one of the safeguards on the body's immune system. Sometimes the immune system starts attacking other parts of the body, which can cause serious or even life-threatening problems in the lungs, intestines, liver, hormone-making glands, kidneys, or other organs.

It's very important to report any new side effects to your cancer care team promptly. If serious side effects do occur, treatment may need to be stopped and you may get high doses of corticosteroids to suppress your immune system.

# More information about immunotherapy

To learn more about how drugs that work on the immune system are used to treat cancer, see <u>Cancer Immunotherapy</u><sup>2</sup>.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u><sup>3</sup>.

# **Hyperlinks**

- 1. <u>www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy/cancer-vaccines.html</u>
- 2. <u>www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html</u>
- 3. www.cancer.org/cancer/managing-cancer/side-effects.html

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# Targeted Drug Therapy for Prostate Cancer

As researchers have learned more about some of the changes inside prostate cancer cells that help them grow, they have developed newer types of drugs that target these changes.

- How targeted drugs work
- PARP inhibitors
- More information about targeted therapy

#### How targeted drugs work

Targeted drugs attack specific parts of cancer cells that make them different from normal cells. This is different from chemotherapy (chemo) and hormone therapy drugs. Targeted drugs sometimes work when these other types of drugs don't, and they often have different side effects.

Like chemo and hormone therapy, these drugs enter the bloodstream and reach almost all areas of the body, which makes them useful against some cancers that have spread to distant parts of the body.

# **PARP** inhibitors

PARP (poly(ADP)-ribose polymerase) enzymes are proteins inside cells that normally help repair damaged DNA.

Some other proteins inside cells (including the *BRCA1* and *BRCA2* proteins) also help repair DNA, but in a different way. Mutations (changes) in genes that code for one of

these DNA repair proteins can stop them from working like they should.

Drugs called **PARP inhibitors**, which block the PARP proteins, make it very hard for tumor cells with an abnormal DNA repair gene (including a *BRCA1* or *BRCA2* gene change) to repair their damaged DNA, which often leads to the death of these cells.

These drugs are only likely to be helpful if the cancer cells have changes in one of the DNA repair genes. Your doctor will likely test your blood or your cancer cells to be sure the cells have a DNA repair gene change before starting treatment with a PARP inhibitor.

These drugs are taken by mouth as pills or capsules, typically once or twice a day. They are given along with some type of hormone therapy, such as an LHRH agonist or after an orchiectomy.

**Rucaparib (Rubraca)** can be used to treat metastatic, castration-resistant prostate cancer (mCRPC) that has grown after treatment with taxane chemotherapy (such as docetaxel or cabazitaxel) and hormone therapy, and when the cancer cells have a change in one of the *BRCA* genes.

Olaparib (Lynparza) can be used to treat mCRPC, either:

- Along with the hormone therapy drug abiraterone (and a steroid drug such as prednisone), if the cancer cells have changes in one of the *BRCA* genes
- By itself, if the cancer has grown after getting a hormone therapy drug such as enzalutamide or abiraterone, and the cancer cells have a change in one of the BRCA genes (or other DNA repair genes known as homologous recombinant repair (HRR) genes\*)

**Talazoparib (Talzenna)** can be used along with the hormone therapy drug enzalutamide to treat mCRPC, if the cancer cells have a change (mutation) in a homologous recombination repair (HRR) gene.\*

**Niraparib plus abiraterone (Akeega)** can be used (along with the steroid drug prednisone) to treat mCRPC if the cancer cells have a change in one of the *BRCA* genes.

\*HRR genes include: *BRCA1, BRCA2, ATM, ATR, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCA, FANCL, MLH1, MRE11A, NBN, PALB2, RAD51B, RAD51C, RAD51D,* and *RAD54L*.

#### Side effects of PARP inhibitors

Some of the more common side effects of these drugs can include nausea, vomiting, diarrhea, fatigue, loss of appetite, low red blood cell counts (anemia), constipation, skin rash, abnormal liver blood tests, low blood platelet counts, cough and shortness of breath. Other side effects are also possible.

Rarely, some people treated with these drugs might develop a blood cancer later on, such as <u>myelodysplastic syndrome<sup>1</sup></u> or <u>acute myeloid leukemia<sup>2</sup></u>.

Some men taking olaparib might develop blood clots in the lungs or legs.

#### More information about targeted therapy

To learn more about how targeted drugs are used to treat cancer, see <u>Targeted Cancer</u> <u>Therapy</u><sup>3</sup>.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u><sup>4</sup>.

# **Hyperlinks**

- 1. <u>www.cancer.org/cancer/types/myelodysplastic-syndrome.html</u>
- 2. www.cancer.org/cancer/types/acute-myeloid-leukemia.html
- 3. www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html
- 4. <u>www.cancer.org/cancer/managing-cancer/side-effects.html</u>

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# Treatments for Prostate Cancer Spread to Bones

If prostate cancer spreads (metastasizes) to other parts of the body, it nearly always goes to the bones first. If the cancer has grown outside the prostate, a major goal of treatment is preventing or slowing the spread of the cancer to the bones. If the cancer has already reached the bones, controlling or relieving pain and other complications is also a very important part of treatment.

- Dealing with bone metastasis
- Bisphosphonates
- Denosumab
- Corticosteroids
- External radiation therapy
- Radiopharmaceuticals
- Ablative treatments
- Surgery
- Pain medicines

# Dealing with bone metastasis

<u>Bone metastasis</u><sup>1</sup> can be painful and can cause other problems, such as fractures (breaks), spinal cord compression (when a tumor presses on the spinal cord), or high blood calcium levels, which can be dangerous or even life threatening.

Treatments such as hormone therapy, chemotherapy, targeted drugs, and immunotherapy may help with this, but other treatments specifically target bone metastasis and the problems it may cause.

# **Bisphosphonates**

Bisphosphonates are drugs that work by slowing down bone cells called **osteoclasts**. These cells normally break down the hard mineral structure of bones to help keep them healthy. When prostate cancer spreads to the bones, osteoclasts can become overactive, which can cause problems. Bisphosphonates can be used:

- To help relieve pain and high calcium levels caused by cancer that has spread to the bones
- To help slow the growth of cancer that has spread to the bones and help delay or prevent fractures
- To help strengthen bones in men who are getting hormone therapy

**Zoledronic acid (Zometa, other names)** is a commonly used bisphosphonate for prostate cancer. This drug 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.

Sometimes other bisphosphonates are used to treat prostate cancer that has spread to bone.

**Side effects of bisphosphonates** can include flu-like symptoms and bone or joint pain. These drugs can also cause kidney problems, so patients with poor kidney function might not be able to be treated with these medicines.

A rare but very serious side effect of these drugs is **osteonecrosis of the jaw (ONJ)**. With this condition, part of the jawbone loses its blood supply and dies. This can lead to tooth loss and infections of the jawbone that are hard to treat. Some people develop ONJ when dental work is done during treatment. Men are often advised 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 ONJ.

# Denosumab

**Denosumab (Xgeva, Prolia)** is another drug that can help when prostate cancer spreads to the bones. Like bisphosphonates, denosumab also blocks osteoclasts, but it does so in a different way. This drug can be used:

• To help prevent or delay problems like fractures in men whose cancer has already spread to the bones. It may be helpful even if zoledronic acid is no longer working.

• To help strengthen bones in men who are getting hormone therapy

This drug is injected under the skin. It is typically given between once every 4 weeks to once every 6 months, depending on why it's being used. Men given this drug are often advised to take a supplement containing calcium and vitamin D to prevent problems with low calcium levels.

Common **side effects of denosumab** include <u>nausea</u><sup>2</sup>, <u>diarrhea</u><sup>3</sup>, and feeling <u>weak</u><sup>4</sup> or <u>tired</u><sup>5</sup>. Like the bisphosphonates, denosumab can also cause ONJ, so doctors recommend taking the same precautions (such as having teeth and jaw problems treated **before** starting the drug).

# Corticosteroids

Corticosteroid drugs (such as prednisone and dexamethasone) might also help relieve bone pain in some men. They also can help lower PSA levels.

These drugs are often already a part of treatment for prostate cancer that has spread, as they're often given along with certain chemo or hormone therapy drugs.

# **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, and prevent paralysis. In some centers this is done with stereotactic body radiation therapy (SBRT), which allows the treatment to be completed more quickly.

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 damaged bones (like those containing cancer spread). Once there, they give off radiation that kills cancer cells.

These drugs can be used to treat prostate cancer that has spread to many bones. Unlike external beam radiation, these drugs can reach all the affected bones at the same time.

The radiopharmaceuticals that can be used to treat prostate cancer that has spread to the bones include:

- Radium-223 (Xofigo)
- Strontium-89 (Metastron)
- Samarium-153 (Quadramet)

All of these drugs can help relieve pain caused by bone metastases.

Radium-223 has also been shown to help men who have prostate cancer spread only to their bones (as opposed to spread to other organs such as the lungs) to live longer. For these men, radium-223 may be an early part of treatment.

The major side effect of these drugs is a <u>decrease in blood cell counts</u><sup>6</sup>, which could increase risks for <u>infections</u><sup>7</sup> or <u>bleeding</u><sup>8</sup>, especially if your counts are already low. Other side effects are also possible, so ask your doctor what you can expect.

#### Ablative treatments

These treatments focus extreme heat or cold on bone tumors to ablate (destroy) them. Ablative treatments might be an option if there are only a few tumors, especially if radiation isn't helpful. One drawback with some ablative techniques is that they require a probe to be inserted into the tumor, which isn't always possible with bone tumors.

Examples of ablative treatments include:

**High-intensity focused ultrasound (HIFU):** For this technique, a probe outside the body precisely focuses ultrasound waves on the tumor to heat and destroy the cancer cells.

**Radiofrequency ablation (RFA):** In this approach, a thin metal probe is inserted into the tumor. An electric current is then run through the probe, which heats the tip to destroy the cancer cells.

**Cryoablation (cryotherapy):** For this treatment, a thin, hollow metal probe is inserted into the tumor. Very cold gases are passed into the probe, which freezes the cancer cells. The tumor is then thawed, and the process is typically repeated.

Other ablative techniques now being studied include microwave ablation, laser ablation,

and irreversible electroporation (IRE).

# Surgery

Kyphoplasty is a minor surgery to stabilize a painful collapsed bone in a spine weakened by prostate cancer. During this procedure, a small incision is made in the middle of the back, and a balloon is placed into the weak spinal bone. The balloon is first filled with air and then a cement-like mixture (which will harden) to stabilize the bone and spine.

# **Pain medicines**

When properly prescribed, pain medicines are very effective. Pain medicines work best when they're taken on a regular schedule. They don't work as well if they're only used when the pain becomes severe.

If you have bone pain from prostate cancer, it's very important that it's treated. This can help you feel better and let you focus on the things 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.

To learn more about pain, how to talk to your cancer care team about it, and the different ways to manage it, see <u>Cancer Pain</u><sup>9</sup>.

# **Hyperlinks**

- 1. www.cancer.org/cancer/managing-cancer/advanced-cancer/bone-metastases.html
- 2. <u>www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/nausea-and-vomiting.html</u>
- 3. <u>www.cancer.org/cancer/managing-cancer/side-effects/stool-or-urine-</u> <u>changes/diarrhea.html</u>
- 4. <u>www.cancer.org/cancer/managing-cancer/side-effects/fatigue-weakness-sleep.html</u>
- 5. <u>www.cancer.org/cancer/managing-cancer/side-effects/fatigue-weakness-sleep.html</u>
- 6. <u>www.cancer.org/cancer/managing-cancer/side-effects/low-blood-counts.html</u>

- 7. <u>www.cancer.org/cancer/managing-cancer/side-effects/infections.html</u>
- 8. <u>www.cancer.org/cancer/managing-cancer/side-effects/low-blood-</u> <u>counts/bleeding.html</u>
- 9. <u>www.cancer.org/cancer/managing-cancer/side-effects/pain.html</u>

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# **Considering Treatment Options for Early Prostate Cancer**

For most men diagnosed with prostate cancer, the cancer is found while it's still at an early <u>stage</u><sup>1</sup>, when it's small and hasn't spread beyond the prostate gland. These men often have several treatment options to consider.

- Deciding which option might be best for you
- Getting help with treatment decisions
- Some things to consider when choosing among treatments

# Deciding which option might be best for you

Not every man with prostate cancer needs to be treated right away. If you have earlystage prostate cancer, there are many factors to take into account, such as your age and overall health, and the likelihood that the cancer will cause problems for you, before deciding on what to do. You should also think about the possible side effects of treatment and how likely they are to bother you. Some men, for example, may want to avoid possible side effects, such as <u>incontinence</u><sup>2</sup> or <u>erection problems</u><sup>3</sup>, for as long as possible. Other men might be less concerned about these side effects and more concerned about removing or destroying the cancer.

If you're 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 <u>chronic disease</u><sup>4</sup> that will probably not lead to your death (although it may cause symptoms you want to avoid). You may be more inclined to consider <u>active surveillance or observation</u> (watchful waiting), and less likely to lean toward treatments such as <u>radiation</u> and <u>surgery</u>, which may cause bothersome side effects. Of course, age alone is not the most important factor when making your choice. Many older men are still in good mental and physical shape, while some younger men may not be as healthy.

If you are younger and otherwise healthy, you might be more willing to accept possible side effects of treatment if they offer you the best chance to cure the cancer. Most doctors believe that surgery, external radiation, and brachytherapy all have about the same cure rates for the earliest-stage prostate cancers. However, each type of treatment has its own risks and benefits that should be considered.

Choosing among treatment options can be complicated even further by the development of newer types of treatment (such as newer surgery and radiation therapy

approaches), which may provide even more options to consider.

Another consideration is the development in recent years of **focal therapies**, which are treatments aimed only at the area of the prostate containing the tumor. This is unlike surgery and most forms of radiation therapy, which affect the whole prostate. (For more on focal treatments, see Cryotherapy, HIFU, and Other Ablative Treatments for Prostate Cancer.) These types of treatments might be less likely to cause side effects, such as incontinence and erection problems. They might be additional options for some men who aren't comfortable with active surveillance but who are concerned about possible side effects from surgery or radiation.

Many of these newer treatments are now available, but there is very little long-term data on them, which means it's hard to compare their effectiveness and safety to more established treatments.

# Getting help with treatment decisions

Making such a complex decision is often hard to do by yourself. You might find it helps to talk with your family and friends before making a decision. You might also find it helpful to speak with other men who have faced or are currently facing the same issues. The American Cancer Society and other organizations offer support programs where you can 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 <u>Patient Programs and Services<sup>5</sup></u>.

It's important to know 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 might also want to consider getting more than one medical opinion, perhaps even from different types of doctors. It is natural for doctors to favor the forms of treatment they're most comfortable with. For example, surgical specialists such as urologists might favor surgery, while radiation oncologists might lean more toward radiation therapy. In the same way, doctors specializing in newer types of treatment may be more likely to recommend their therapies. Talking to each of them might 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.

#### Some things to consider when choosing among treatments

Before deciding on treatment, here are some 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?
- Would you be comfortable with active surveillance (or observation), even if it means you might have more anxiety and need more frequent follow-up visits and tests in the future?
- If it's an option, would you consider a form of focal therapy to treat your cancer, which might have fewer side effects than surgery or radiation but is not yet well proven?
- Do you need to know right away whether your doctor was able to get all of the cancer out (as a result of surgery)? Or are you comfortable with perhaps not knowing the results of treatment for a while (as is the case in radiation therapy or focal therapies) if it means not having to have surgery?
- Are you more inclined to go with a newer technology (such as proton beam radiation therapy), which in theory might have some advantages, even if it's not yet well proven?
- Which potential treatment side effects (incontinence, erection problems, bowel problems) might be most distressing to you?
- How important for you are issues like the amount of time spent in treatment or recovery?
- If your initial choice of treatment isn't successful, what would your treatment options be at that point?

Many men find it very stressful to have to choose between treatment options, and they might worry they will choose the "wrong" one. But in many cases, there is no single option that is clearly better than all the others. What's more, unless the cancer is known to be growing quickly or has other concerning features, it most likely won't need to be treated right away, so it's important to take your time to consider your options carefully when deciding which one is right for you.

# Hyperlinks

- 1. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-</u> <u>staging/staging.html</u>
- 2. <u>www.cancer.org/cancer/managing-cancer/side-effects/stool-or-urine-</u> <u>changes/bladder-incontinence.html</u>
- 3. www.cancer.org/cancer/managing-cancer/side-effects/fertility-and-sexual-side-

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- 5. www.cancer.org/support-programs-and-services.html

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# Initial Treatment of Prostate Cancer, by Stage and Risk Group

The <u>stage</u><sup>1</sup> of your cancer is one of the most important factors in choosing the best way to treat it. Prostate cancer is staged based on the extent of the cancer (using T, N, and M categories) and the <u>PSA level and Gleason score (Grade Group)</u><sup>2</sup> when it is first

diagnosed.

- Very-low-risk group
- Low-risk group
- Favorable intermediate-risk group
- Unfavorable intermediate-risk group
- High- or very-high-risk group
- Stage IV
- Prostate cancer that has spread or come back

For prostate cancers that haven't spread (stages I to III), doctors also use <u>risk groups</u><sup>3</sup> (based on how far the prostate tumor has grown, PSA level, grade, and prostate biopsy results) and sometimes special lab tests to help guide treatment options. Risk groups range from very low-risk to very high-risk. **Cancers in the lower-risk groups have a smaller chance of growing and spreading compared to those in higher-risk groups.** 

Other factors, such as your age, overall health, life expectancy, and personal preferences are also important when looking at treatment options. This is especially true for early-stage cancers, where you might have several options.

You might want to ask which factors your doctor is considering when discussing your treatment options. There is also some variability in what different doctors consider to be "standard" options, so some doctors might recommend options different from those listed here.

Taking part in a <u>clinical trial</u><sup>4</sup> of newer treatments is also an option for many men with prostate cancer.

# Very-low-risk group

These prostate cancers are very unlikely to grow and spread, even if they aren't treated. For men whose cancers are in this group, active surveillance is typically recommended. (For men who have medical problems that might shorten their lifespan, observation, which is a less intense form of monitoring, might be an option as well.) This is because these tumors are unlikely to cause any harm, while treatments such as radiation and surgery can have side effects that can affect a man's quality of life. If the cancer starts to show signs of growing at some point, treatments such as surgery or radiation can then be considered. For men who aren't comfortable with just monitoring the cancer and choose to start treatment right away, radiation therapy (external beam or brachytherapy) or surgery (radical prostatectomy) may be options.

Another option for some men who prefer to treat the cancer might be some type of focal therapy, such as cryotherapy or high-intensity focused ultrasound (HIFU). However, most expert groups don't recommend these as a first treatment, unless surgery and radiation aren't good options. This is mainly because there isn't enough long-term data yet to show if these treatments are as effective as surgery or radiation.

If surgery is done and it finds concerning features in the cancer, your doctor might recommend external radiation therapy to the prostate bed (the area where the prostate was before it was removed), possibly along with hormone therapy.

# Low-risk group

Most men whose prostate cancers are in the low-risk group will be offered active surveillance (or observation, for men who have other serious health issues that might affect their lifespan), since very few of these cancers will spread to distant parts of the body. If the cancer starts to show signs of growing at some point, treatments such as surgery or radiation can then be considered.

Other options, depending on a man's preferences, might include radiation therapy (external beam or brachytherapy) or surgery (radical prostatectomy).

Another option for some men who prefer to treat the cancer might be some type of focal therapy, such as cryotherapy or high-intensity focused ultrasound (HIFU). However, most expert groups don't recommend these as a first treatment, unless surgery and radiation aren't good options. This is mainly because there isn't enough long-term data yet to show if these treatments are as effective as surgery or radiation.

If surgery is done and it finds concerning features in the cancer, your doctor might recommend external radiation therapy to the prostate bed (the area where the prostate was before it was removed), possibly along with hormone therapy.

# Favorable intermediate-risk group

These cancers are slightly more likely to grow and spread. Initial treatment options for men with these cancers might include:

Active surveillance

- Surgery (radical prostatectomy, possibly with the removal of nearby lymph nodes)
- Radiation therapy (external beam or brachytherapy)

Another option for some men who prefer to treat the cancer might be some type of focal therapy, such as cryotherapy or high-intensity focused ultrasound (HIFU). However, most expert groups don't recommend these as a first treatment, unless surgery and radiation aren't good options. This is mainly because there isn't enough long-term data yet to show if these treatments are as effective as surgery or radiation.

If surgery is done and it finds concerning features in the prostate cancer, your doctor might recommend external radiation therapy to the prostate bed (the area where the prostate was before it was removed), possibly along with hormone therapy. If cancer is found in the lymph nodes, hormone therapy might be recommended, possibly along with external radiation.

Men who have other serious medical problems that might affect their life span may choose a less aggressive first treatment such as radiation alone, or less intensive monitoring (observation).

# Unfavorable intermediate-risk group

Initial treatment options for men with cancers in this risk group might include:

- Surgery (radical prostatectomy, along with the removal of nearby lymph nodes)
- External radiation therapy plus hormone therapy
- External radiation plus brachytherapy (possibly along with hormone therapy)

If surgery is done and it finds concerning features in the prostate cancer, your doctor might recommend external radiation therapy to the prostate bed (the area where the prostate was before it was removed), possibly along with hormone therapy. If cancer is found in the lymph nodes, hormone therapy might be recommended, possibly along with external radiation.

Men who have other serious medical problems that might affect their lifespan may choose a less aggressive first treatment such as radiation therapy (possibly with hormone therapy), or less intensive monitoring (observation).

# High- or very-high-risk group

For men with cancers that are at high or very high risk of growing and spreading, treatment options might include:

- Radiation therapy (external beam radiation, either alone or with brachytherapy) along with hormone therapy (typically for 1 to 3 years). For cancers in the very-high-risk group, the newer hormone drug abiraterone is often included as well.
- Surgery (radical prostatectomy, along with the removal of nearby lymph nodes)

If surgery is done and it finds concerning features in the prostate cancer, your doctor might recommend external radiation therapy to the prostate bed (the area where the prostate was before it was removed), possibly along with hormone therapy. If cancer is found in the lymph nodes, hormone therapy might be recommended, possibly along with external radiation.

Men who have other serious medical problems that might affect their lifespan may choose a less aggressive first treatment, such as external radiation therapy or hormone therapy, or less intensive monitoring (observation).

# Stage IV

**Stage IVA** cancers have already spread to nearby lymph nodes (but not to distant parts of the body) when the cancer is first found. For men who don't have other serious medical problems that might affect their life span or who are having symptoms from the cancer, options include:

- External beam radiation treatment with hormone therapy (which often includes the newer hormone drug abiraterone)
- Hormone therapy (which might include abiraterone)
- Surgery (radical prostatectomy, along with the removal of nearby lymph nodes), only in men who are most likely to benefit from it

If surgery is done and it finds concerning features in the prostate cancer, your doctor might recommend external radiation therapy to the prostate bed (the area where the prostate was before it was removed), possibly along with hormone therapy. If cancer is found in the lymph nodes, hormone therapy might be recommended, possibly along with external radiation.

Men who have other serious medical problems that might affect their life span and who aren't having symptoms may choose a less aggressive first treatment such as hormone therapy, or less intensive monitoring (observation).

**Stage IVB** cancers have spread to distant organs such as the bones when the cancer is found. Most stage IVB cancers can't be cured, but they are treatable. The goals of treatment are to keep the cancer under control for as long as possible and to improve a man's quality of life. Initial treatment options may include:

- Hormone therapy (which typically includes a newer hormone drug, such as abiraterone, apalutamide, or enzalutamide)
- Hormone therapy (which typically includes a newer hormone drug, such as abiraterone or darolutamide) along with chemotherapy (usually docetaxel), especially if there is a lot of cancer in the body
- Hormone therapy with external beam radiation to the tumor in the prostate
- Surgery (TURP) to relieve <u>symptoms</u><sup>5</sup>, such as bleeding or urinary obstruction
- Observation (for those who are older or have other serious health issues and do not have major symptoms from the cancer)
- Taking part in a <u>clinical trial</u><sup>6</sup> of newer treatments

Treatment of stage IV prostate cancer may also include treatments to help prevent or relieve symptoms, such as pain from bone metastases. This can be done with external radiation (including stereotactic body radiation therapy, or SBRT) or with drugs like denosumab (Xgeva), a bisphosphonate such as zoledronic acid (Zometa), or a radiopharmaceutical such as radium-223, strontium-89, or samarium-153.

# Prostate cancer that has spread or come back

The options above are for the initial treatment of different risk groups and stages of prostate cancer. But if the cancer continues to grow and spread or if it comes back, other treatments might be options, such as immunotherapy, targeted drug therapy, chemotherapy, or other forms of hormone therapy. (See Treating Prostate Cancer That Doesn't Go Away or Comes Back After Treatment.)

# **Hyperlinks**

- 1. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-</u> staging/staging.html
- 2. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</u>

- 3. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-</u> <u>staging/staging.html</u>
- 4. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-</u> <u>trials.html</u>
- 5. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/signs-</u> <u>symptoms.html</u>
- 6. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-</u> <u>trials.html</u>

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# Following PSA Levels During and After Prostate Cancer Treatment

A man's <u>prostate-specific antigen (PSA)</u><sup>1</sup> blood level is often a good indicator of how effective treatment has been.

- · PSA level as a tool to monitor prostate cancer
- During active surveillance or watchful waiting (observation)
- After surgery (prostatectomy)
- After radiation therapy
- During treatment for advanced prostate cancer

### PSA level as a tool to monitor prostate cancer

Generally speaking, your PSA level should get very low after treatment. But PSA results only give a limited amount of information, and sometimes doctors aren't sure what they mean.

Before starting treatment, you might want to ask your doctor what your PSA level is expected to be during and after treatment, and what levels might cause concern. It's important to know that the PSA level is only one part of the overall picture. Other factors can also play a role in determining if cancer is still there, if it is growing, or if it has come back.

It's also important to know that PSA levels can sometimes fluctuate a bit on their own, even during or after treatment, so they may not always be an accurate sign of what is happening with your cancer. Understandably, many men being treated for prostate cancer are very concerned about even small changes in their PSA levels. The PSA level is an important tool to monitor the cancer, but not every rise in PSA means that the cancer is growing and requires treatment right away.

### During active surveillance or watchful waiting (observation)

If you choose active surveillance or observation, your PSA level will be monitored closely (most likely along with other tests) to help decide if the cancer is growing and if treatment should be considered.

Not all doctors agree on exactly what PSA level might require further action (such as a <u>prostate biopsy</u><sup>2</sup> or treatment), whether it's a set number or how quickly it's rising. Again, talk to your doctor so you understand what change in your PSA might be considered cause for concern.

# After surgery (prostatectomy)

Your PSA should fall to a very low or even undetectable level within a couple of months after radical prostatectomy. Because some PSA can 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 checking the PSA level.

Some men might worry if their PSA is still detectable even at a very low level after surgery, but this does not always mean cancer is still in the body. Modern PSA blood tests can detect even tiny amounts of PSA, but these amounts might not always be significant, especially if they are not rising over time. It could just mean that you have some cells in the body making PSA, but these aren't necessarily cancer cells.

Still, having any detectable PSA after surgery can be stressful for men and their loved ones. If your PSA is still detectable after surgery, even at a very low level, talk to your doctor about what it might mean, and what the best course of action might be. Some doctors advise following such low PSA levels over time to get a better idea of what's going on. Other doctors might recommend further treatment.

If your PSA increases after surgery, your doctor might also want to know how fast it is rising. Some evidence shows that faster-rising PSA levels may be more of a concern. Men who have a shorter **PSA doubling time** (the time it takes for the PSA level to double) tend to have a worse prognosis (outlook) compared to men with longer PSA doubling times.

## After radiation therapy

Radiation therapy doesn't kill all of the cells in the prostate gland, so it's not expected to cause the PSA to drop to an undetectable level. The remaining normal prostate cells will still make some PSA.

The pattern of the drop in PSA after radiation therapy is also different from after surgery. PSA levels after radiation tend to drop slowly, and they might 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 cause for closer monitoring, but it might not mean that the cancer is still there (or has returned), as PSA levels can fluctuate slightly from time to time. However, a PSA that is rising on consecutive tests after treatment might indicate that cancer is still there. Some medical groups have proposed that if the PSA rises more than 2 ng/mL above the lowest level reached, further treatment should be considered, but some doctors might advise tests to look for cancer in the body even if the PSA has not yet risen this much.

As is the case after surgery, if your PSA begins to rise after radiation treatment, your doctor might also want to know how fast it is rising. Men who have a shorter **PSA doubling time** (the time it takes for the PSA level to double) tend to have a worse prognosis (outlook) compared to men with longer PSA doubling times.

There is also a phenomenon called a **PSA bounce** that sometimes happens after external beam radiation and brachytherapy. The PSA rises slightly for a short time within the first couple of years after treatment, but then goes back down. Doctors aren't sure why this happens, but it doesn't seem to affect a man's prognosis.

### During treatment for advanced prostate cancer

When treatments such as hormone therapy, chemotherapy, or immunotherapy are used for more advanced prostate cancer, the PSA level can help show how well the treatment is working or when it might be time to try a different 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're having <u>symptoms</u><sup>3</sup> from your cancer and whether <u>imaging tests</u><sup>4</sup> show it is growing, 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 the direction and speed with which 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 levels and feel just fine, while other men with low PSA levels might have symptoms.

# **Hyperlinks**

- 1. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 2. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 3. www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/signssymptoms.html
- 4. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</u>

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# Treating Prostate Cancer That Doesn't Go Away or Comes Back After Treatment

If you've been treated for prostate cancer and your <u>prostate-specific antigen (PSA)</u><sup>1</sup> blood level or another test shows that your prostate cancer has not been cured or has come back (recurred), further treatment can often still be helpful.

- Follow-up treatment options
- Cancer that is thought to still be in or around the prostate (or that isn't seen on imaging tests)
- Cancer that has reached nearby areas
- · Cancer that has spread to other parts of the body
- · Castration-resistant and hormone-refractory prostate cancer

### Follow-up treatment options

Follow-up treatment will depend on where the cancer is thought to be, what treatment(s) you've already had, and other factors. Imaging tests (such as MRI, PET scans, or bone scans) or biopsies may be done to get a better idea about where the cancer is and which treatments are most likely to be helpful.

# Cancer that is thought to still be in or around the prostate (or that isn't seen on imaging tests)

If the cancer is still thought to be just in the area of the prostate, a second attempt to cure it might be possible.

After surgery: If you've had a radical prostatectomy, radiation therapy to the area where the prostate was might be an option, sometimes along with hormone therapy (which might include a newer hormone drug such as abiraterone).

**After radiation therapy:** If your first treatment was radiation, treatment options might include surgery (radical prostatectomy) or some type of ablative therapy (such as cryotherapy or high-intensity focused ultrasound (HIFU)). However, when these treatments are done after radiation, they carry a higher risk for side effects such as incontinence<sup>2</sup>. Getting radiation therapy again might not be a good option because of the increased risk of serious side effects, although in some cases brachytherapy may be an option as a second treatment after external radiation.

Sometimes when the cancer doesn't go away (or when it comes back) after the first treatment, it might not be clear exactly where the remaining cancer is in the body. If the only sign of cancer is a **biochemical recurrence** (a rising PSA level alone, without cancer being seen on imaging tests), another option for some men might be active surveillance instead of treatment. Prostate cancer often grows slowly, so even if it does come back, it might not cause problems for many years, at which time further treatment could then be considered.

Factors such as how quickly the PSA is rising and the original <u>Gleason score</u><sup>3</sup> of the cancer can help predict how soon the cancer might show up in distant parts of the body and cause problems. If the PSA is going up very quickly, some doctors might recommend that you start treatment even before the cancer can be seen on tests or causes <u>symptoms</u><sup>4</sup>.

Observation (less intensive monitoring) might be a more appealing option for some groups of men, such as those who are older and in whom the PSA level is rising slowly. Still, not all men might be comfortable with this approach.

If the PSA is rising quickly enough to warrant treatment, but localized treatments (such as surgery, radiation therapy, or ablative therapy) aren't likely to be helpful, hormone therapy with a drug such as enzalutamide is often the next option. If one type of hormone therapy isn't helpful, another can be tried (see "Castrate-resistant prostate cancer," below).

### Cancer that has reached nearby areas

If tests show that the cancer has spread to the pelvic area (but hasn't yet spread to other parts of the body), treatment options will likely depend on what type of treatment you've had.

After surgery: If you've had a radical prostatectomy, radiation therapy to the pelvic area might be an option, typically along with hormone therapy (which might include a newer hormone drug such as abiraterone).

After radiation therapy: If your first treatment was radiation, treatment options might include hormone therapy or monitoring the cancer (and then treating it with hormone therapy if it becomes necessary). Other options for some men might include surgery to remove the pelvic lymph nodes (pelvic lymph node dissection, or PLND) or radiation to the pelvic lymph nodes (if it hasn't been done already).

### Cancer that has spread to other parts of the body

If the cancer has spread to other parts of the body, it will most likely go to the bones or other lymph nodes outside of the pelvis first. Much less often the cancer might spread to the liver or other organs.

When prostate cancer has spread to other parts of the body (including the bones), hormone therapy is usually the preferred treatment. But while it's often very effective for a time, it isn't likely to cure the cancer, and at some point it might stop working. Usually the first treatment is a luteinizing hormone-releasing hormone (LHRH) agonist (often along with a first-generation anti-androgen), LHRH antagonist, or orchiectomy. It might be used:

- Along with a newer hormone drug, such as abiraterone, apalutamide, or enzalutamide
- Along with a chemotherapy drug (usually docetaxel) and a newer hormone drug, such as abiraterone or darolutamide
- By itself

For tumors in the bones, other treatments aimed at <u>bone metastases</u><sup>5</sup> might be used as well.

### Castration-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 usually becomes less effective over time. Doctors use different terms to describe cancers that are no longer responding to hormones.

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

antagonist) is keeping the testosterone level in the body as low as what would be expected if the testicles were removed (called *castrate levels*). The cancer might 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 with prostate cancer that is still growing despite initial hormone therapy (CRPC) now have many more treatment options than they had in the past.

If the prostate cancer cells haven't been tested for gene or protein changes that might affect treatment options, that might be done at this time.

If a first-generation anti-androgen (flutamide, bicalutamide, or nilutamide) was not part of the initial hormone therapy, it may be 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) seems to help sometimes.

One of the newer hormone drugs may be added to the existing hormone therapy, especially if the cancer is causing few or no symptoms. These include abiraterone (Zytiga), enzalutamide (Xtandi), apalutamide (Erleada), and darolutamide (Nubeqa). Other less commonly used options might include ketoconazole, estrogens (female hormones), and corticosteroids.

The prostate cancer vaccine sipuleucel-T (Provenge) is another option for men whose cancer is causing few or no symptoms. This might not lower PSA levels, but it can often help men live longer.

For cancers that are no longer responding to initial hormone therapy and are causing symptoms, several options might be available. If it hasn't been used already, chemotherapy with the drug docetaxel is often the first choice because it has been shown to help men live longer, as well as to reduce pain. If docetaxel doesn't work or stops working, other chemo drugs, such as cabazitaxel, may help.

Depending on which treatments a man has had, other options at some point might include:

- A different type of hormone therapy, such as abiraterone or enzalutamide (if they haven't been tried yet)
- The radiopharmaceutical lutetium Lu 177 vipivotide tetraxetan (Pluvicto), if the cancer cells have the PSMA protein

- A targeted therapy drug, such as rucaparib (Rubraca), olaparib (Lynparza), talazoparib (Talzenna), or niraparib plus abiraterone (Akeega), typically along with hormone therapy, if the cancer cells have a change (mutation) in a DNA repair gene such as *BRCA1* or *BRCA2*
- Immunotherapy with pembrolizumab (Keytruda) or dostarlimab (Jemperli), if the cancer cells have certain gene changes (MSI-H, dMMR, or high TMB)

Several types of treatment might be helpful if cancer has spread to the bones. These include:

- Drugs that affect bone cells, such as bisphosphonates or denosumab
- External radiation therapy (including stereotactic body radiation therapy, or SBRT), especially if there are only a few bone tumors
- Radiopharmaceutical drugs, which can often be helpful if the cancer is more widespread
- Ablative treatments, which focus extreme heat or cold on bone tumors to ablate (destroy) them. These might be an option if there are only a few tumors, especially if radiation isn't helpful.

Many medicines can also help relieve pain. If you are having <u>pain<sup>6</sup></u> from prostate cancer, make sure your doctor and health care team know about it.

Several promising new medicines are now being tested against castration-resistant and hormone-refractory prostate cancer. Because these cancers can become hard to treat, men with these cancers might want to consider exploring new options by taking part in <u>clinical trials</u><sup>7</sup>.

## Hyperlinks

- 1. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 2. <u>www.cancer.org/cancer/managing-cancer/side-effects/stool-or-urine-</u> <u>changes/bladder-incontinence.html</u>
- 3. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 4. www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/signs-

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- 5. www.cancer.org/cancer/managing-cancer/advanced-cancer/bone-metastases.html
- 6. www.cancer.org/cancer/managing-cancer/side-effects/pain.html
- 7. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-</u> <u>trials.html</u>

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