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# **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 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, social workers, rehabilitation specialists, and other health professionals.

Health Professionals Associated with Cancer Care

### 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 is 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 Prostate Cancer Treatment Options

#### 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-of-the 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. Still, they're not right for everyone.

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.

Clinical Trials

### Considering complementary and alternative methods

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

Complementary methods refer to treatments that are used along with your regular medical care. Alternative treatments are used instead of a doctor's medical treatment. Although some of these 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.

Complementary and Integrative Medicine

### 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 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 National Cancer Information Center at 1-800-227-2345 and speak with one of our trained 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 and 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.

#### If Cancer Treatments Stop Working

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

- When are these options used?
- Observation or active surveillance vs. treatment

Because prostate cancer often grows very slowly, some men (especially those who are older or have other serious health problems) who have it might never need treatment. Instead, their doctors may recommend **observation** (sometimes called **watchful waiting**) or **active surveillance**.

The terms active surveillance and observation mean something slightly different:

- Active surveillance is often used to mean monitoring the cancer closely. Usually this includes a doctor visit with a <u>prostate-specific antigen (PSA) blood test</u><sup>1</sup> about every 6 months and a <u>digital rectal exam (DRE)</u><sup>2</sup> at least once a year. <u>Prostate biopsies</u><sup>3</sup> and <u>imaging tests</u><sup>4</sup> may be done every 1 to 3 years as well. If your test results change, your doctor would then talk to you about treatment options to try and cure the cancer.
- Observation (watchful waiting) is sometimes used to describe a less intensive
  type of follow-up that may mean fewer tests and relying more on changes in a
  man's <u>symptoms</u><sup>5</sup> to decide if treatment is needed. This treatment is most often
  meant to control symptoms from the cancer, but not to cure it.

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 if your cancer:

- Isn't causing any symptoms
- Is expected to grow slowly (based on <u>Gleason score</u><sup>6</sup>)
- Is small
- Is just in the prostate
- Is associated with low PSA level (<10ng/ml)</li>

They are not likely to be good options if you have a fast-growing cancer (for example, a high Gleason score) or if the cancer is likely to have spread outside the prostate (based on PSA levels). Men who are young and healthy are less likely to be offered observation, out of concern that the cancer might become a problem over the next 20 or 30 years.

Observation and active surveillance are reasonable options for some men with slow-growing cancers because it is not known if treating the cancer with surgery or radiation will actually help them live longer. In active surveillance, only men whose cancer is growing (and therefore have a more serious form of cancer) are treated. For some men, these treatments have risks and side effects that may outweigh their benefits. Other men are not comfortable with observation or active surveillance because the cancer might grow and spread, limiting treatment options and the possibility of treating the cancer successfully. Some men accept the possible side effects of treatments to try to remove or destroy the cancer.

#### Observation or active surveillance vs. treatment

A few large studies have compared observation (**watchful waiting**) (where men were treated only if they developed symptoms from their cancer) and surgery for early-stage prostate cancer, but the evidence from these studies has been mixed. Some have found that men who have surgery might live longer, while others have not found a difference in survival.

So far, a few studies have compared **active surveillance** to treatments such as surgery or radiation therapy. Men who undergo surgery or radiation do not appear to live longer than those that undergo active surveillance, but their cancer might stay away longer and spread less.

## **Hyperlinks**

- 1. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 2. <a href="www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html">www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</a>
- 3. <a href="https://www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html">www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</a>

- 4. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 5. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/signs-symptoms.html</u>
- 6. <a href="https://www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html">www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</a>

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# **Surgery for Prostate Cancer**

- Open or laparoscopic radical prostatectomy
- Risks of prostate surgery
- Side effects of prostate surgery
- 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.

The main type of surgery for prostate cancer is a **radical prostatectomy**. In this operation, the surgeon removes the entire prostate gland plus some of the tissue around it, including the <u>seminal vesicles</u><sup>1</sup>.

## Open or laparoscopic radical prostatectomy

In the more traditional approach to prostatectomy, called anopen prostatectomy, the surgeon operates through a single long skin incision (cut) to remove the prostate and nearby tissues. This type of surgery is done less often than in the past.

In a laparoscopic prostatectomy, the surgeon makes several smaller incisions and uses special long surgical tools to remove the prostate. The surgeon either holds the tools directly, or uses a control panel to precisely move robotic arms that hold the tools. This approach to prostatectomy has become more common in recent years. If done by experienced surgeons, the laparoscopic radical prostatectomy can give results similar to the open approach.

#### Open prostatectomy

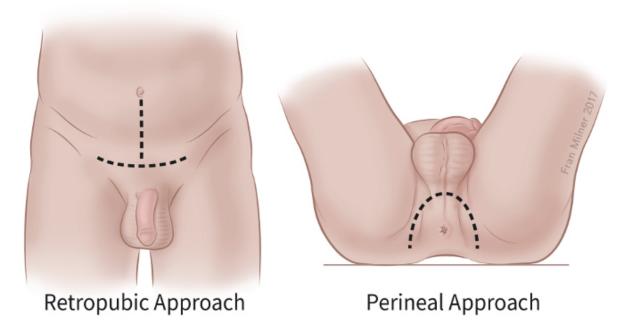
#### Radical retropubic prostatectomy

For this open 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.

If there is 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 also remove some of these lymph nodes at this time (known as a pelvic lymph node dissection). The nodes are sent to the lab to see if they have cancer cells in them. 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.

After the prostate is removed, 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. But it is often a shorter operation and might be an option if you aren't concerned about erections and you don't need lymph nodes removed. It also might be used if you have other medical conditions that make

retropubic surgery difficult for you. It can be just as curative as the retropubic approach if done correctly. The perineal operation may result in less pain and an easier recovery than the retropubic prostatectomy.

After the surgery, while you are still under anesthesia, a catheter will be put in your penis to help drain your bladder. The catheter usually stays in place for 1 to 2 weeks while you are healing. You will be able to urinate on your own after the catheter is removed.

You will probably stay in the hospital for a few days after the surgery, and your activities will be limited for several weeks.

### Laparoscopic prostatectomy

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

#### Laparoscopic radical prostatectomy

For a laparoscopic radical prostatectomy(LRP), the surgeon inserts special long instruments through several small incisions in the abdominal wall to remove the prostate. One of the instruments has a small video camera on the end, which lets the surgeon see inside the body.

Laparoscopic prostatectomy has some advantages over open radical prostatectomy, including less blood loss and pain, shorter hospital stays (usually no more than a day), faster recovery times, and the catheter will need to remain in the bladder for less time.

The rates of major side effects from LRP, such as erection problems and trouble holding urine (incontinence) seem to be about the same as for open prostatectomies. Recovery of bladder control may be delayed slightly with this approach.

Even though more long-term studies are needed to compare side effects and chances of recurrence between open prostatectomy and LRP, success of either procedure seems to be determined mainly by the experience and skill of the surgeon.

#### Robotic-assisted laparoscopic radical prostatectomy

In this approach, also known as **robotic prostatectomy**, the laparoscopic surgery 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 in the patient's abdomen.

Robotic prostatectomy has advantages over the open approach in terms of less pain, blood loss, and recovery time. But in terms of the side effects men are most concerned about, such as urinary or erection problems, there doesn't seem to be a difference between robotic prostatectomy and other approaches.

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

#### 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 into the urethra to the level of the prostate. Once it is in place, either electricity is passed through a wire to heat it or a laser is used to cut or vaporize the tissue. Spinal anesthesia (which numbs the lower half of your body) or general anesthesia (where you are asleep) is used.

The operation usually takes about an hour. After surgery, a catheter (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.

## Risks of prostate surgery

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.

In extremely rare cases, a man can die because of complications of this operation. Your risk depends, in part, on your overall health, your age, and the skill of your surgical team.

## Side effects of prostate surgery

The major possible side effects of radical prostatectomy are **urinary incontinence** (being unable to control urine) and **erectile dysfunction** (impotence; problems getting or keeping erections). These side effects can also occur with other forms of prostate cancer treatment.

**Urinary incontinence:** You may not be able to control your urine or you may have leakage or dribbling. Being incontinent can affect you not only physically but emotionally and socially as well. 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, normal bladder control usually returns within several weeks or months. This recovery usually occurs slowly over time.

Doctors can't predict for sure how any man will be affected after surgery. In general, older men tend to have more incontinence problems than younger men. 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 and 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 on 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. All men can expect some decrease in the ability to have an erection, but the younger you are, the more likely it is that you will keep this ability.

Surgeons who do many radical prostatectomies tend to report lower impotence rates than doctors who do the surgery less often. A wide range of impotency 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 up to 2 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.

Most 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. 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 are headache, flushing (skin becomes red and feels warm), upset stomach, light sensitivity, and runny or stuffy nose. Rarely, these drugs can cause vision problems, possibly even blindness. Some other drugs such as nitrates, which are drugs 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 mechanical
  pumps are placed over the penis. The air is sucked out of the pump, which draws
  blood into the penis to produce an erection. The erection is maintained after the
  pump is removed by a strong rubber band placed at the base of the penis. The
  band is removed 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>Sexuality for</u> the Man With Cancer.<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, orgasm becomes less intense or goes away completely. Less often, men report pain with orgasm.

Loss of fertility: Radical prostatectomy 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 Fertility and Men With Cancer<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 lymphedema<sup>8</sup> page.

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

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

## 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 Managing Cancer-related Side Effects<sup>10</sup>.

## **Hyperlinks**

- 1. <a href="https://www.cancer.org/cancer/types/prostate-cancer/about/what-is-prostate-cancer.html">www.cancer.org/cancer/types/prostate-cancer/about/what-is-prostate-cancer.html</a>
- 2. www.cancer.org/cancer/diagnosis-staging/lymph-nodes-and-cancer.html
- 3. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 4. <a href="https://www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html">www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</a>
- 5. <u>www.cancer.org/cancer/managing-cancer/side-effects/stool-or-urine-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**

- Types of radiation therapy
- External beam radiation therapy (EBRT)
- Brachytherapy (internal radiation therapy)
- Radiopharmaceuticals
- More information about radiation therapy

Radiation therapy uses high-energy rays or particles to kill cancer cells. Depending on the <a href="stage">stage</a>¹ 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 and is low grade<sup>2</sup>. Cure rates for men with these types of cancers are about the same as those for men treated with radical prostatectomy.
- As part of the first treatment (along with hormone therapy) for cancers that have

grown outside the prostate gland and into nearby tissues.

- If the cancer is not removed completely or comes back (recurs) in the area of the prostate after surgery.
- If the cancer is advanced, to help keep the cancer 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, or to help relieve symptoms such as bone pain if the cancer has spread to a specific area of bone.

You will usually go for treatment 5 days a week in an outpatient center for at least several weeks, depending on why the radiation is being given. Each treatment is much like getting an x-ray. The radiation is stronger than that used for an x-ray, but the procedure typically is painless. Each treatment lasts only a few minutes, although the setup time — getting you into place for treatment — takes longer.

Newer EBRT techniques focus the radiation more precisely on the tumor. 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 it 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 beam 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.

Some newer radiation machines have imaging scanners built into them. This advance, known as **image guided radiation therapy (IGRT)**, lets the doctor take pictures of the prostate just before giving the radiation to make minor adjustments in aiming. This appears to help deliver the radiation even more precisely and results 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 over just a few minutes. Although this can be more convenient for the patient, it hasn't yet been shown to be more effective than regular IMRT.

#### Stereotactic body radiation therapy (SBRT)

This technique 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 over just a few days.

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

The main advantage of SBRT over IMRT is that the treatment takes less time (days instead of weeks). The side effects, though, are not better. In fact, some research has shown that some side effects might actually be worse with SBRT than with IMRT.

#### 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 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. Unlike x-rays, which release energy both before and after they hit their target, protons cause little damage to tissues they pass through and release their energy only after traveling a certain distance. This means that proton beam radiation can, in theory, deliver more radiation to the prostate while doing less damage to nearby normal tissues. Proton beam radiation can be aimed with techniques similar to 3D-CRT and IMRT.

Although in theory proton beam therapy might be more effective than using x-rays, so far studies have not 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:** Radiation can irritate the rectum and cause a condition called **radiation proctitis**. This can lead to <u>diarrhea</u><sup>4</sup>, sometimes with blood in the stool, and rectal leakage. Most of these problems go away over time, but in rare cases normal bowel function does not return. 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 is put between the rectum and the prostate before treatment to act like a spacer to 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 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 <u>surgery</u> 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 tube that carries urine from the bladder out of the body (the urethra) may become very narrow or even close off, which is known as a urethralstricture. This might require further treatment to open it up again.

**Erection problems, including impotence:** After a few years, the impotence rate after radiation is about the same as that after surgery. Problems with erections usually do not occur right after radiation therapy but slowly develop over time. This is different from surgery, where impotence occurs immediately and may get better over time.

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>Sexuality</u> for the Man 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 <a href="https://lymphedema">lymphedema</a> 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 relatively slow growing (low-grade).
- 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 not be possible to place the seeds into all of the correct locations. One way to get around this may be to get a few months of hormone therapy beforehand to shrink the prostate.

Imaging tests such as transrectal <u>ultrasound</u><sup>8</sup>, <u>CT scans</u><sup>9</sup>, or <u>MRI</u><sup>10</sup> are 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 asleep), 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

In this approach, pellets (seeds) of radioactive material (such as iodine-125 or palladium-103) are placed inside thin needles, which are inserted through the skin in the area between the scrotum and anus and into the prostate. The pellets are left in place as the needles are removed and give off low doses of radiation for weeks or months. Radiation from the seeds travels a very short distance, so the seeds can 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 outside the prostate (for example, if you have a higher <u>Gleason score</u><sup>11</sup>).

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

This technique is done less often. It leaves higher doses of radiation in place 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. Radioactive 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 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

**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, this is uncommon and doesn't seem to cause any ill effects.

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

**Bowel problems:** 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) is not a common side effect. 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 gets better over time. Rarely, the urethra may actually close off (known as a urethral stricture) and need to be opened with a catheter or surgery.

**Erection problems:** Some studies have found rates of erection problems to be lower after brachytherapy, but other studies have found that the rates were no different than with external beam radiation or surgery. 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>Sexuality for the Man With Cancer</u><sup>12</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</u><sup>13</sup> 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 the 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:

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

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 Radiation Therapy<sup>14</sup>.

To learn about some of the side effects listed here and how to manage them,

see Managing Cancer-related Side Effects<sup>15</sup>.

## **Hyperlinks**

- 1. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/staging.html</u>
- 2. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 3. <u>www.cancer.org/cancer/managing-cancer/treatment-types/radiation/external-beam-radiation-therapy.html</u>
- 4. <a href="www.cancer.org/cancer/managing-cancer/side-effects/stool-or-urine-changes/diarrhea.html">www.cancer.org/cancer/managing-cancer/side-effects/stool-or-urine-changes/diarrhea.html</a>
- 5. <u>www.cancer.org/cancer/managing-cancer/side-effects/fertility-and-sexual-side-effects/sexuality-for-men-with-cancer.html</u>
- 6. www.cancer.org/cancer/managing-cancer/side-effects/fatigue.html
- 7. www.cancer.org/cancer/managing-cancer/side-effects/swelling/lymphedema.html
- 8. <u>www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/ultrasound-for-cancer.html</u>
- 9. <u>www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/ct-scan-for-cancer.html</u>
- 10. <a href="https://www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/mri-for-cancer.html">www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/mri-for-cancer.html</a>
- 11. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 12. <u>www.cancer.org/cancer/managing-cancer/side-effects/fertility-and-sexual-side-effects/sexuality-for-men-with-cancer.html</u>
- 13. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 14. www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html
- 15. www.cancer.org/cancer/managing-cancer/side-effects.html

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# **Cryotherapy for Prostate Cancer**

When is cryotherapy used?

- How is cryotherapy done?
- Possible side effects of cryotherapy

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

## 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 cannot have surgery or radiation therapy. However, most doctors do not use cryotherapy as the first treatment for prostate cancer..

## How is cryotherapy done?

This type of procedure requires spinal or epidural anesthesia (the lower half of your body is numbed) or general anesthesia (you are asleep).

The doctor uses <u>transrectal ultrasound (TRUS)</u><sup>1</sup> to guide several 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 freeze and destroy the prostate. To be sure the prostate is destroyed without too much damage to nearby tissues, the doctor carefully watches the ultrasound during the procedure. Warm saltwater is passed through a catheter in the urethra during the procedure 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 go home the same day.

Cryotherapy is less invasive than surgery, so there is usually less blood loss, a shorter hospital stay, shorter recovery period, and less pain. But compared with surgery or radiation therapy, doctors know much less about the long-term effectiveness of cryotherapy. And as with brachytherapy, this may not be a good option for men with large prostate glands.

## Possible side effects of cryotherapy

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

Most men have <u>blood in their urine</u><sup>2</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>Sexuality for the Man With Cancer</u><sup>3</sup>.

<u>Urinary incontinence</u><sup>4</sup> (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.

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

## **Hyperlinks**

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

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# **Hormone Therapy for Prostate Cancer**

- When is hormone therapy used?
- Types of hormone therapy
- Current issues in hormone therapy
- More information about hormone therapy

Hormone therapy is also called **androgen suppression therapy**. 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.

Androgens stimulate prostate cancer cells to 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 often makes prostate cancers shrink or grow more slowly for a time. But hormone therapy alone does not cure prostate cancer.

## When is hormone therapy used?

Hormone therapy may be used:

- 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
- If the cancer remains or comes back after treatment with surgery or radiation therapy
- Along with radiation therapy as the initial treatment, if you are at higher risk of the cancer coming back after treatment (based on a high <u>Gleason score</u><sup>1</sup>, high <u>PSA level</u><sup>2</sup>, and/or growth of the cancer outside the prostate)
- Before radiation to try to shrink the cancer to make treatment more effective

## Types of hormone therapy

Several types of hormone therapy can be used to treat prostate cancer.

### Treatment to lower testicular androgen levels

**Androgen deprivation therapy**, also called **ADT**, uses 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 choose treatment with drugs that lower hormone levels (such as an LHRH agonist or antagonist) instead.

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 inserted into 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)
- Goserelin (Zoladex)
- Triptorelin (Trelstar)
- Leuprolide mesylate (Camcevi)

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. Men whose cancer has spread to the bones may have bone pain. Men whose prostate gland has not been removed may have trouble urinating. If the cancer has spread to the spine, even a short-term increase in tumor growth as a result of the flare could 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 side effects can include:

- Reduced or absent sexual desire<sup>3</sup>
- Erectile dysfunction (impotence)<sup>4</sup>
- 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)<sup>5</sup>
- Decreased mental sharpness<sup>6</sup>
- Loss of muscle mass
- Weight gain<sup>7</sup>
- Fatique<sup>8</sup>
- Increased cholesterol levels
- Depression<sup>9</sup>

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<sup>10</sup>, but this has not been studied thoroughly. Still, hormone therapy does seem to lead to memory problems in some men. These problems are rarely severe, and most often affect only some types of memory. More studies are being done to look at this issue.

#### 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 (protein) called CYP17, which helps stop these cells 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>11</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. It 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, 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, <u>upset stomach</u><sup>12</sup>, and <u>diarrhea</u><sup>13</sup>. Ketoconazole can cause elevated liver blood tests, nausea, vomiting, gynecomastia (enlargement of breast tissue in men) and a skin rash.

#### Drugs that stop androgens from working

### Anti-androgens

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 are drugs that also connect to these receptors, keeping the androgens from causing tumor growth. Anti-androgens are also sometimes called **androgen receptor antagonists**.

Drugs of this type include:

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

They are taken daily as pills.

In the United States, anti-androgens are not often used by themselves:

- 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).
   There is still some debate as to whether CAB is more effective in this setting than
  using orchiectomy or an LHRH agonist alone. If there is a benefit, it appears to be
  small.
- 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 **anti-androgen 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, but they may have fewer <u>sexual side effects</u><sup>14</sup>. When these drugs are used alone, sexual desire and erections can often be maintained. When these drugs are given to men already being treated with LHRH agonists, <u>diarrhea</u><sup>15</sup> is the major side effect. <u>Nausea</u><sup>16</sup>, liver problems, and <u>tiredness</u><sup>17</sup> can also occur.

#### Newer anti-androgens

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

- All 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 (CRPC), described below).
- **Enzalutamide** can also be used for metastatic prostate cancer (cancer that has spread), whether it is castration-resistant or castration-sensitive (still responding to other forms of hormone therapy).
- Apalutamide and darolutamide can also be used for metastatic castrationsensitive prostate cancer (CSPC), also known as hormone-sensitive prostate cancer (HSPC), described below.

These drugs are taken as pills each day.

**Side effects** can include <u>diarrhea</u><sup>18</sup>, <u>fatigue</u><sup>19</sup>, 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 <u>more likely to fall</u><sup>20</sup>, 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. Still, 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 is not having any symptoms. Some studies have shown 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

Most prostate cancers treated with hormone therapy become resistant to this treatment over a period of months or years. Some doctors believe that constant androgen suppression 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 treat patients with androgen deprivation (orchiectomy or an LHRH agonist or antagonist) plus an anti-androgen. Some studies have suggested this may be more helpful than androgen deprivation alone, but others have not. Most doctors are not convinced there's enough evidence that this combined therapy is better than starting with one drug alone when treating prostate cancer that has spread to other parts of the body.

#### 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 hormone-sensitive 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>21</sup>.

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects<sup>22</sup>.

# **Hyperlinks**

- www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/howdiagnosed.html
- 2. <a href="www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html">www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</a>
- 3. <u>www.cancer.org/cancer/managing-cancer/side-effects/fertility-and-sexual-side-effects/sexuality-for-men-with-cancer.html</u>
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- 5. www.cancer.org/cancer/managing-cancer/side-effects/low-blood-counts.html
- 6. <a href="https://www.cancer.org/cancer/managing-cancer/side-effects/changes-in-mood-or-thinking.html">www.cancer.org/cancer/managing-cancer/side-effects/changes-in-mood-or-thinking.html</a>
- 7. <a href="www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/weight-changes.html">www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/weight-changes.html</a>
- 8. www.cancer.org/cancer/managing-cancer/side-effects/fatigue.html
- 9. <u>www.cancer.org/cancer/managing-cancer/side-effects/changes-in-mood-or-thinking.html</u>
- 10. <u>www.cancer.org/cancer/managing-cancer/side-effects/changes-in-mood-or-thinking.html</u>
- 11. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 12. <a href="https://www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/nausea-and-vomiting.html">www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/nausea-and-vomiting.html</a>
- 13. <a href="www.cancer.org/cancer/managing-cancer/side-effects/stool-or-urine-changes/diarrhea.html">www.cancer.org/cancer/managing-cancer/side-effects/stool-or-urine-changes/diarrhea.html</a>
- 14. <u>www.cancer.org/cancer/managing-cancer/side-effects/fertility-and-sexual-side-effects.html</u>
- 15. <u>www.cancer.org/cancer/managing-cancer/side-effects/stool-or-urine-changes/diarrhea.html</u>

- 16. <a href="https://www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/nausea-and-vomiting.html">www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/nausea-and-vomiting.html</a>
- 17. <a href="https://www.cancer.org/cancer/managing-cancer/side-effects/fatigue.html">www.cancer.org/cancer/managing-cancer/side-effects/fatigue.html</a>
- 18. <a href="www.cancer.org/cancer/managing-cancer/side-effects/stool-or-urine-changes/diarrhea.html">www.cancer.org/cancer/managing-cancer/side-effects/stool-or-urine-changes/diarrhea.html</a>
- 19. www.cancer.org/cancer/managing-cancer/side-effects/fatigue.html
- 20. www.cancer.org/cancer/managing-cancer/side-effects/falls.html
- 21. www.cancer.org/cancer/managing-cancer/treatment-types/hormone-therapy.html
- 22. www.cancer.org/cancer/managing-cancer/side-effects.html

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# **Chemotherapy for Prostate Cancer**

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

#### More information about chemotherapy

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

### When is chemotherapy used?

Chemo is sometimes used if prostate cancer has spread outside the prostate gland and hormone therapy isn't working. Recent research has also shown that chemo might be helpful if given along with hormone therapy. Chemo is not, however, 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 (Taxotere)
- Cabazitaxel (Jevtana)
- Mitoxantrone (Novantrone)
- Estramustine (Emcyt)

In most cases, the first chemo drug given is docetaxel, combined with the steroid drug prednisone. If this does not work (or stops working), cabazitaxel is often the next chemo drug tried (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 slow the cancer's growth and also reduce <a href="mayer-symptoms">symptoms</a><sup>1</sup>, resulting in a better quality of life. Still, chemo is very unlikely to cure prostate cancer.

Other chemo drugs being studied for use in prostate cancer include carboplatin, oxaliplatin, and cisplatin.

# How is chemotherapy given?

Chemo drugs for prostate cancer are typically given into a vein (IV), either 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.

Often, a slightly larger and sturdier IV is required in the vein system to administer chemo. They 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 different 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 2 or 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.

The length of treatment for advanced prostate cancer is based on how well it is 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<sup>3</sup>
- Mouth sores<sup>4</sup>
- Loss of appetite<sup>5</sup>
- Nausea and vomiting<sup>6</sup>
- Diarrhea<sup>7</sup>
- Increased chance of infections<sup>8</sup> (from having too few white blood cells)
- Easy <u>bruising or bleeding</u><sup>9</sup> (from having too few blood platelets)
- Fatique<sup>10</sup> (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 help 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 <u>peripheral neuropathy</u><sup>11</sup>), which can cause numbness, tingling, or
  burning sensations in the hands or feet.
- Mitoxantrone can, very rarely, cause <u>leukemia</u><sup>12</sup> several years later.
- Estramustine carries an increased risk of blood clots.

If you notice any <u>side effects</u><sup>13</sup> 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 Chemotherapy<sup>14</sup>.

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects<sup>15</sup>.

# **Hyperlinks**

- 1. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/signs-symptoms.html</u>
- 2. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/tubes-lines-ports-catheters.html</u>
- 3. www.cancer.org/cancer/managing-cancer/side-effects/hair-skin-nails/hair-loss.html
- 4. <a href="www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/mouth-sores.html">www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/mouth-sores.html</a>
- 5. <u>www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/poor-</u>

- appetite.html
- 6. <u>www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/nausea-and-vomiting.html</u>
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- 10. www.cancer.org/cancer/managing-cancer/side-effects/fatigue.html
- 11. <u>www.cancer.org/cancer/managing-cancer/side-effects/nervous-system/peripheral-neuropathy.html</u>
- 12. <u>www.cancer.org/cancer/survivorship/long-term-health-concerns/second-cancers-in-adults.html</u>
- 13. www.cancer.org/cancer/managing-cancer/side-effects.html
- 14. www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html
- 15. www.cancer.org/cancer/managing-cancer/side-effects.html

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# Immunotherapy for Prostate Cancer

- Cancer vaccine
- · Possible side effects of vaccine treatment
- Immune checkpoint inhibitors
- More information about immunotherapy

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

**Sipuleucel-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 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 it seems to help men live 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 <u>fever</u>, chills, <u>fatigue</u>, back and joint <u>pain</u>, <u>nausea</u>, 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 <u>problems breathing</u> 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 hold a lot of promise as cancer treatments.

Drugs called checkpoint inhibitors can be used for people whose prostate cancer cells have tested positive for specific gene changes, such as a high level of microsatellite instability (MSI-H), or changes in one of the mismatch repair (MMR) genes. Changes in MSI or in MMR genes (or both) are often seen in people with Lynch syndrome<sup>7</sup>.

The drugs are used for people whose cancer starts growing again after chemotherapy. They might also be used to treat people whose cancer can't be removed with surgery, has come back (recurred) after treatment, or has spread to other parts of the body (metastasized).

#### PD-1 inhibitor

Pembrolizumab (Keytruda) is a drug that targets PD-1, a checkpoint protein on immune system cells called T cells, that normally helps keep these cells from attacking normal cells in the body. By blocking PD-1, this drug boosts the immune response against prostate cancer cells. It has shown promising results in some men with prostate cancer and continues to be studied.

This drug is given as an intravenous (IV) infusion every 2 or 3 weeks.

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

Other, more serious side effects occur less often. This drug works by basically removing the brakes from 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 health 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>8</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>9</sup>.

# **Hyperlinks**

- 1. www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html
- 2. www.cancer.org/cancer/managing-cancer/side-effects/low-blood-counts/fever.html
- 3. www.cancer.org/cancer/managing-cancer/side-effects/fatigue.html
- 4. www.cancer.org/cancer/managing-cancer/side-effects/pain.html
- 5. <u>www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/nausea-and-vomiting.html</u>
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- 7. www.cancer.org/cancer/risk-prevention/genetics/family-cancer-syndromes.html
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# Targeted Drug Therapy for Prostate Cancer

- PARP inhibitors
- More information about targeted therapy

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. These targeted drugs work differently from chemotherapy (chemo) and hormone therapy drugs. They 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

Rucaparib (Rubraca) and olaparib (Lynparza) are drugs known as a **PARP** (poly(ADP)-ribose polymerase) inhibitors. PARP enzymes normally help repair damaged DNA inside cells.

The proteins coded for by the *BRCA* genes (*BRCA1* and *BRCA2*) also normally help repair DNA, but in a different way, and mutations (changes) in one of these genes can stop the BRCA proteins from working like they should.

By blocking the PARP proteins as well, these drugs make it very hard for tumor cells with an abnormal *BRCA* gene to repair damaged DNA, which often leads to the death of these cells.

Your doctor will likely test your blood or saliva and your cancer cells to be sure the cells have a *BRCA* gene change before starting treatment with a PARP inhibitor.

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

**Rucaparib (Rubraca)** can be used to treat metastatic, castration-resistant prostate cancer 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 metastatic, castration-resistant prostate cancer, 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)

**Talazoparib (Talzenna)** can be used to treat metastatic, castration-resistant prostate cancer that have homologous recombination repair (HRR) gene mutation(s) and have not received any prior treatment for castration-resistant disease. Talazoparib has been approved to be given with enzalutamide once per day. HRR genes include: ATM, ATR, BRCA1, BRCA2, CDK12, CHEK2, FANCA, MLH1, MRE11A, NBN, PALB2, and RAD51C.

#### Side effects of PARP inhibitors

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.

Rarely, some people treated with these drugs might develop a blood cancer later on, such as <u>myelodysplastic syndrome</u><sup>1</sup> or <u>acute myeloid leukemia</u><sup>2</sup>. 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 Managing Cancer-related Side Effects<sup>4</sup>.

# **Hyperlinks**

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

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# **Treatments for Prostate Cancer Spread** to Bones

- Bisphosphonates
- Denosumab
- Corticosteroids

- External radiation therapy
- Radiopharmaceuticals
- Surgery
- Pain medicines

If prostate cancer spreads to other parts of the body, it nearly always goes to the bones first. Bone metastasis¹ can be painful and can cause other problems, such as fractures (breaks), spinal cord compression (an area of cancer is pressing on the spinal cord), or high blood calcium levels, which can be dangerous or even life threatening.

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

Treatments such as hormone therapy, chemotherapy, and vaccines 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. Osteoclasts often become overactive when prostate cancer spreads to the bones, 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)** is a commonly used bisphosphonate for prostate cancer. This drug is given as an intravenous (IV) injection, usually either once every 3 or 4 weeks, or once every 12 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.

Bisphosphonates can have side effects, including flu-like symptoms and bone or joint pain<sup>2</sup>. They 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 jaw bone loses its blood supply and dies. This can lead to tooth loss and infections of the jaw bone that are hard to treat. Some people develop ONJ when dental work is done during treatment. Many times men are 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)** is another drug that can help when prostate cancer spreads to bone. Like the 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 every 4 weeks. 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 include <u>nausea</u><sup>3</sup>, <u>diarrhea</u><sup>4</sup>, and feeling <u>weak</u><sup>5</sup> or <u>tired</u><sup>6</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**

Some studies suggest that corticosteroid drugs(such as prednisone and dexamethasone) can help relieve bone pain in some men. They also can help lower PSA levels. These drugs are often already a part of prostate cancer treatment that has spread.

# **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. 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 spread to bone include:

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

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>7</sup>, which could increase risks for <u>infections</u><sup>8</sup> or <u>bleeding</u><sup>9</sup>, especially if your counts are already low. Other side effects have also been seen, so ask your doctor what you can expect.

# **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>10</sup>.

# **Hyperlinks**

- 1. www.cancer.org/cancer/managing-cancer/advanced-cancer/bone-metastases.html
- 2. <a href="www.cancer.org/cancer/managing-cancer/side-effects/pain/facts-about-cancer-pain.html">www.cancer.org/cancer/managing-cancer/side-effects/pain/facts-about-cancer-pain.html</a>
- 3. <a href="https://www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/nausea-and-vomiting.html">www.cancer.org/cancer/managing-cancer/side-effects/eating-problems/nausea-and-vomiting.html</a>
- 4. <a href="www.cancer.org/cancer/managing-cancer/side-effects/stool-or-urine-changes/diarrhea.html">www.cancer.org/cancer/managing-cancer/side-effects/stool-or-urine-changes/diarrhea.html</a>
- 5. www.cancer.org/cancer/managing-cancer/side-effects/fatigue.html
- 6. www.cancer.org/cancer/managing-cancer/side-effects/fatigue.html
- 7. www.cancer.org/cancer/managing-cancer/side-effects/low-blood-counts.html
- 8. <u>www.cancer.org/cancer/managing-cancer/side-effects/low-blood-counts/infections.html</u>
- 9. <u>www.cancer.org/cancer/managing-cancer/side-effects/low-blood-counts/bleeding.html</u>
- 10. <a href="https://www.cancer.org/cancer/managing-cancer/side-effects/pain.html">www.cancer.org/cancer/managing-cancer/side-effects/pain.html</a>

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# **Considering Prostate Cancer Treatment Options**

- Getting help with treatment decisions
- Some things to consider when choosing among treatments

For most men diagnosed with prostate cancer, the cancer is found while it's still at an early stage -- it's small and has not spread beyond the prostate gland. These men often have several treatment options to consider.

Not every man with prostate cancer needs to be treated right away. If you have early-stage prostate cancer, there are many factors such as your age and general health, and the likelihood that the cancer will cause problems for you to consider before deciding 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 <a href="incontinence">incontinence</a> or <a href="incontinence">erection problems</a><sup>2</sup> for as long as possible. Other men are 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 <a href="chronic disease">chronic disease</a><sup>3</sup> that will probably not lead to your death but may cause symptoms you want to avoid. You may think more about watchful waiting or active surveillance, and less about treatments that are likely to cause major side effects, such as radiation and surgery. Of course, age itself is not necessarily the best reason for your choice. Many men are in good mental and physical shape at age 70, while some younger men may not be as healthy.

If you are younger and otherwise healthy, you might be more willing to accept possible side effects of treatment if they offer you the best chance for cure. 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 risks and benefits that should be considered.

Choosing among treatment options is complicated even further by the development of newer types of surgery (such as robotic-assisted prostatectomy) and radiation therapy (such as proton beam radiation) in recent years. Many of these seem very promising, but there is very little long-term data on them, which means comparing their effectiveness and possible side effects is difficult. These newer treatments can also only be done in centers with specialized equipment and trained doctors.

# 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 <a href="Find Support Programs">Find Support Programs</a> and Services<sup>4</sup>.

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. For early-stage cancers, it is natural for surgical specialists, such as urologists, to favor surgery and for radiation oncologists to lean more toward radiation therapy. 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 watchful waiting or active surveillance, even if it
  means you might have more anxiety and need more frequent follow-up
  appointments in the future?
- 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 not knowing the results of treatment for a while (as is the case in radiation therapy) if it means not having to have surgery?
- Do you prefer to go with the newest technology (such as robotic surgery or proton beam radiation therapy), which might have some advantages? Or do you prefer to go with better proven treatments that doctors might have more experience with?
- Which potential treatment side effects (incontinence, impotence, bowel problems) might be most distressing to you?
- How important for you are issues like the amount of time spent in treatment or recovery?
- If your initial treatment is not successful, what would your options be at that point?

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

# **Hyperlinks**

- 1. <u>www.cancer.org/cancer/managing-cancer/side-effects/stool-or-urine-changes/bladder-incontinence.html</u>
- 2. <u>www.cancer.org/cancer/managing-cancer/side-effects/fertility-and-sexual-side-effects/sexuality-for-men-with-cancer.html</u>
- 3. <u>www.cancer.org/cancer/survivorship/long-term-health-concerns/cancer-as-a-chronic-illness.html</u>
- 4. www.cancer.org/support-programs-and-services.html

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

- Very-low-risk group
- Low-risk group
- Intermediate-risk group

- High-risk group
- Very-high-risk group
- Stage IVA
- Stage IVB

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.

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 group, and prostate biopsy results) to help determine if more tests should be done and to help guide treatment options. Risk groups range from very-low-risk to very-high-risk, with **cancers** in the lower risk groups having 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. In fact, many doctors determine a man's possible treatment options based not just on the stage, but on the risk of cancer coming back (recurrence) after the initial treatment and on the man's life expectancy.

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

For men in this group without any other serious health problems that may limit their lifespan, active surveillance is often recommended because these tumors are unlikely to harm the patient, while radiation and surgery can have side effects that can change a man's quality of life.

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

For men who have medical problems that might shorten their lifespan, observation is another possibility.

#### Low-risk group

Most men whose prostate cancers are in the low-risk group and who don't have serious health issues will be offered active surveillance since very few of these cancers will spread to distant parts of the body. Other options, depending on your preferences, might include radiation therapy (external beam or brachytherapy) or radical prostatectomy. If the findings after surgery show that the cancer has features that make it more likely to come back, then the following treatments might be considered:

- External beam radiation to the prostate bed (the area where the prostate gland used to be before it was removed) with or without hormone therapy OR
- Close follow-up of the PSA levels, with the plan to consider radiation treatment if the PSA level starts to go up.

Observation is often a good option for men whose cancer is not causing any symptoms and who have other serious health problems.

#### Intermediate-risk group

Radiation therapy (external beam or brachytherapy), often with hormone therapy, is an option for men in this group.

A radical prostatectomy with pelvic lymph node dissection (PLND) is also an option. Depending on the findings from surgery, treatments that might be discussed include:

- External beam radiation therapy with or without hormone therapy if the cancer is found in the lymph nodes or if it has features that make it more likely to come back (recur)
- Close follow-up of the PSA level, with the plan to consider radiation treatment if the PSA level starts to rise.

Active surveillance is an option for people in this group whose cancers have favorable features. But there is a slightly higher risk of the cancer spreading compared to getting radiation treatment or radical prostatectomy with PLND as the initial therapy.

Men who have other serious medical problems may choose less aggressive treatment such as radiation alone or observation.

# High-risk group

People with cancer in this group might be offered:

- Radiation therapy (external beam with brachytherapy OR external beam radiation alone) along with hormone therapy for 1 to 3 years.
- Radical prostatectomy with PLND. If cancer is found in the lymph nodes removed during surgery or if it has features that make it more likely to come back (recur), hormone therapy with or without radiation might be recommended. In some cases, instead of radiation or hormone therapy, watching the PSA closely after surgery might be considered, with the plan to consider hormone therapy with or without radiation treatment if the PSA level rises.

For men with other serious health problems and symptoms from their prostate cancer, hormone therapy alone might be a good choice. For men with no symptoms from the cancer and who have major health issues, hormone therapy alone, external beam radiation therapy alone, or observation might be options.

# Very-high-risk group

Treatment options for people in this group include:

- External beam radiation therapy (with or without brachytherapy) along with hormone therapy (ADT) for 1 to 3 years. Sometimes, the chemotherapy drug docetaxel or the hormone drug abiraterone might be added to radiation plus ADT.
- Radical prostatectomy with PLND (especially for younger men). If cancer is found in
  the lymph nodes removed during surgery, hormone therapy with or without external
  beam radiation treatment might be given. Radiation therapy with or without
  hormone therapy might be recommended if the cancer is not found in the lymph
  nodes but does have features that make it more likely to come back (recur). In
  some cases, instead of radiation or hormone therapy, watching the PSA level
  closely after surgery might be done, with the plan to consider hormone therapy with
  or without radiation if the PSA level rises.

For men with no symptoms from the cancer but who have major health issues, treatment options might include hormone therapy alone, external beam radiation therapy alone, or observation.

# **Stage IVA**

Stage IVA cancers have spread to nearby lymph nodes but not to distant parts of the body. For men who are healthy enough to get treatment or have symptoms from the cancer, options include:

- External beam radiation treatment with hormone therapy (ADT, with or without abiraterone)
- Hormone therapy (ADT, with or without abiraterone)
- Radical prostatectomy with PLND. If cancer is found in the lymph nodes removed during surgery or it has features that make it more likely to come back (recur), hormone therapy with or without external beam radiation treatment might be given. In some cases, instead of radiation or hormone therapy, watching the PSA closely after surgery might be done, with the plan to consider hormone therapy with or without radiation if the PSA level starts to go up.

For men with Stage IVA cancer without symptoms or with other serious health problems, observation or hormone therapy alone might be recommended.

# Stage IVB

Stage IVBcancers have spread to distant organs such as the bones. 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 (typically ADT, alone or along with a newer hormone drug)
- Hormone therapy with chemotherapy (usually docetaxel)
- 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<sup>7</sup> from bone metastases. This can be done with external radiation or with drugs like denosumab (Xgeva), a bisphosphonate like zoledronic acid (Zometa), or a radiopharmaceutical such as radium-223, strontium-89, or samarium-153.

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-staging/staging.html</u>
- 2. <a href="www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html">www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</a>
- 3. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/staging.html</u>
- 4. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html</u>
- 5. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/signs-symptoms.html</u>
- 6. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html</u>
- 7. <a href="www.cancer.org/cancer/managing-cancer/side-effects/pain.html">www.cancer.org/cancer/managing-cancer/side-effects/pain.html</a>

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# Following PSA Levels During and After Prostate Cancer Treatment

- During watchful waiting (observation) or active surveillance
- After surgery
- After radiation therapy
- During treatment for advanced prostate cancer

A man's <u>prostate-specific antigen (PSA)</u><sup>1</sup> blood level is often a good indicator of how effective treatment is or has been. Generally speaking, your PSA level should get very low after treatment. But PSA results aren't always reliable, 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 a sign of what is actually

happening with your cancer. Understandably, many men being treated for prostate cancer are very concerned about even very 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. To help limit unnecessary anxiety, be sure you understand what change in your PSA level might concern your doctor.

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

If you choose observation or active surveillance, 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.

Your doctor will watch your PSA level and how quickly it is rising. 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). Again, talk to your doctor so you understand what change in your PSA might be considered cause for concern.

### **After surgery**

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 families. 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 a sign of cancer. Men who have a PSA level that doubles within a 3-month period tend to have a worse prognosis (outlook) compared to men whose PSA level does not double. This is also known as **PSA doubling time**.

#### 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 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 cause 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.

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 <a href="mayingtosymptoms">symptoms</a><sup>3</sup> from your cancer and whether <a href="mayingtosymptoms">imaging tests</a><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 whether it changes, and how quickly it changes. The PSA level itself does not predict whether or not a man will have symptoms or how long he will live. Many men have very high PSA levels and feel just fine. Other men with low PSA levels can 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. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/signs-symptoms.html</u>
- 4. <a href="https://www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html">www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</a>

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

- Cancer that is thought to still be in or around the prostate
- Cancer that clearly has spread
- Castrate-resistant and hormone-refractory prostate cancer

If 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) after the initial treatment, further treatment can often still be helpful. Follow-up treatment will depend on where the cancer is thought to be and what treatment(s) you've already had. Imaging tests such as <u>CT</u><sup>2</sup>, <u>MRI</u><sup>3</sup>, or <u>bone scans</u><sup>4</sup> may be done to get a better idea about where the cancer is.

# Cancer that is thought to still be in or around the prostate

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 might be an option, sometimes along with hormone therapy.

**After radiation therapy:** If your first treatment was radiation, treatment options might include cryotherapy or radical prostatectomy, but when these treatments are done after radiation, they carry a higher risk for side effects such as <u>incontinence</u><sup>5</sup>. Having radiation therapy again is usually not an option because of the increased potential for

serious side effects, although in some cases brachytherapy may be an option as a second treatment after external radiation.

Sometimes it might not be clear exactly where the remaining cancer is in the body. If the only sign of cancer recurrence is a rising PSA level (as opposed to the cancer being seen on imaging tests), another option for some men might be active surveillance instead of active 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 going up and the original <u>Gleason score</u><sup>6</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 symptoms<sup>7</sup>.

Observation might be a more appealing option to certain 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 cryotherapy) aren't likely to be helpful, hormone therapy 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 clearly has spread

If the cancer has spread outside the prostate, it will most likely go to nearby <u>lymph</u> <u>nodes</u><sup>8</sup> first, and then to bones. Much less often the cancer will spread to the liver or other organs.

When prostate cancer has spread to other parts of the body (including the bones), hormone therapy is probably the most effective treatment. But it isn't likely to cure the cancer, and at some point it might stop working. Usually the first treatment is a luteinizing hormone-releasing hormone(LHRH) agonist, LHRH antagonist, or orchiectomy, sometimes along with an anti-androgen drug or abiraterone. Another option might be to get chemotherapy, most often along with the hormone therapy. Other treatments for bone metastases <sup>9</sup> might be used as well.

# Castrate-resistant and hormone-refractory prostate cancer

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

- Castrate-resistant prostate cancer (CRPC) is cancer that is still growing despite
  the fact that hormone therapy (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 whose prostate cancer is still growing despite initial hormone therapy now have many more treatment options than they had even a few years ago.

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

Other forms of hormone therapy may also be helpful for a while, especially if the cancer is causing few or no symptoms. These include abiraterone (Zytiga), enzalutamide (Xtandi), apalutamide (Erleada), darolutamide (Nubeqa), 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. Chemotherapy with the drug docetaxel (Taxotere) 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 (Jevtana), may help.

Other options at some point might include:

- Immunotherapy with pembrolizumab (Keytruda), if the cancer is has certain gene changes (MSI-H or dMMR)
- A different type of hormone therapy, such as abiraterone, enzalutamide, or

- apalutamide (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) or olaparib (Lynparza), possibly along with hormone therapy, if the cancer cells have a BRCA gene mutation

Bisphosphonates or denosumab can often help if the cancer has spread to the bones. These drugs can reduce pain and even slow cancer growth in many men. Other medicines and methods can also help keep pain and other symptoms under control. External radiation therapy can help treat bone pain if it's only in a few spots. Radiopharmaceutical drugs can often reduce pain if it's more widespread, and may also slow the growth of the cancer.

If you are having pain 10 from prostate cancer, make sure your doctor and health care team know about it.

Several promising new medicines are now being tested against prostate cancer, including <u>vaccines</u><sup>11</sup>, <u>monoclonal antibodies</u><sup>12</sup>, and other new types of drugs. Because the ability to treat hormone-refractory prostate cancer is still not good enough, men are encouraged to explore new options by taking part in <u>clinical trials</u><sup>13</sup>.

# **Hyperlinks**

- 1. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 2. <u>www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/ct-scan-for-cancer.html</u>
- 3. <u>www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/mri-for-cancer.html</u>
- 4. <u>www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/nuclear-medicine-scans-for-cancer.html</u>
- 5. <u>www.cancer.org/cancer/managing-cancer/side-effects/stool-or-urine-changes/bladder-incontinence.html</u>
- 6. <u>www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 7. www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/signs-

#### symptoms.html

- 8. www.cancer.org/cancer/diagnosis-staging/lymph-nodes-and-cancer.html
- 9. www.cancer.org/cancer/managing-cancer/advanced-cancer/bone-metastases.html
- 10. <a href="https://www.cancer.org/cancer/managing-cancer/side-effects/pain.html">www.cancer.org/cancer/managing-cancer/side-effects/pain.html</a>
- 11. <u>www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy/cancer-vaccines.html</u>
- 12. www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html
- 13. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html</u>

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