

### Side Effects of Prostate Cancer Treatment

You may be reading this because you (or a loved one) have been diagnosed with prostate cancer and are researching the possible side effects of treatment options. Or perhaps you are currently experiencing side effects of treatment and want to know how you can manage them.

Either way, it is important not to ignore that side effects exist: attending to them is an integral part of your overall treatment and recovery landscape.
For example, one study of chemotherapy patients found that tracking your side effects, and, importantly, reporting them to your health care team, can help you fare better during treatment and live longer, with better quality of life, and fewer emergency room visits.

Because the prostate is close to several vital structures, prostate cancer and its treatments can disrupt normal urinary, bowel, and sexual functioning. The first part of the following information discusses side effects that might be experienced following surgery or radiation therapy for localized or locally advanced prostate cancer. For side effects related to treatment of advanced or metastatic prostate cancer, see page 4.

# Side Effects of Surgery or Radiation Therapy

#### **Urinary Function**

Under normal circumstances, the urinary sphincters (bands of muscle at the base of the bladder and at the base of the prostate) remain tightly shut, preventing urine that's stored in the bladder from leaking out. In prostatectomy – the surgical removal of the prostate – if the sphincter at the base of the bladder is damaged, urinary incontinence or leakage may occur. Nearly all men will have some form of leakage immediately after the surgery, but this will



improve over time and with strengthening exercises. The majority of men regain urinary control within a year; approximately 1 in 5 men will have mild leakage requiring the use of one or more pads per day. This rate depends on patient factors and surgeon experience. Pelvic floor muscle training with a physical therapist can help. In the case that incontinence persists past a year, a urethral sling or artificial urinary sphincter can potentially correct the leakage.

Radiation therapy is targeted to the prostate. Advanced technology directs the dose of radiation away from the bladder and rectum. The urethra runs through the middle of the prostate, so it will receive radiation, but fortunately the urethra is very resistant to radiation therapy, and long-term urinary leakage is rare (less than 1 in 100). However, it can become irritated during and for months after radiation therapy, which usually manifests as a mild increase in urinary frequency and urgency. This can also cause nocturia, or waking up more at night to urinate.

#### **Bowel Function**

Solid waste that is excreted from the body moves slowly down the intestines, and, under normal circumstances, the resultant stool passes through the rectum and then exits via the anus. Damage to the rectum can result in bowel problems, including rectal bleeding, diarrhea, or urgency.

In prostatectomy it is very rare (less than 1%) for men to have altered bowel function after surgery. In rare cases of locally advanced prostate cancer where the cancer invades the rectum, surgery may result in rectal damage, but it isn't often used in these types of cases.

Because the rectum sits right behind the prostate, it may also receive some radiation during treatment. With modern radiation therapy, it is very rare to have moderate or severe bowel problems (less than 3%), and with the use of a device called a rectal spacer, this rate is reduced to near 0%. During radiation therapy you may experience softer stools or diarrhea (less than 10%). These symptoms typically resolve within a few weeks of completing radiation therapy. With modern radiation, only 2% to 3% of men will have bothersome rectal bleeding that may occur months or years after treatment, and with a rectal spacer this rate is reduced to less than 1%. Be sure to discuss with your doctor the types of radiation therapy that are appropriate for you, as older forms of radiation therapy can increase rectal side effects significantly.

#### **Fertility**

After any of the most common prostate cancer treatments—surgery, radiation therapy, or hormone therapy—you are unlikely to be fertile. As part of the surgical removal of the prostate, the seminal vesicles and part of the vas deferens are removed, disrupting the connection to the testes. Orgasm may still occur (without ejaculation) but natural conception will not be possible. Radiation similarly destroys the prostate and seminal vesicles; chemotherapy and hormone therapy are both harmful to sperm production. If you are hoping to father a child in the future, discuss fertility preservation and sperm cryopreservation with your physician before you undergo any treatment.

#### Sexual Function

Regardless of whether the nerves were spared during surgery or whether the most precise dose planning was used during radiation therapy, erectile dysfunction remains the most common side effect after treatment.

This is because the nerves and blood vessels that control the physical aspect of an erection are incredibly delicate, and any trauma to the area can result in changes. Fortunately, beyond short-term side effects, there is also room for great optimism: many excellent treatments for managing erectile function exist on the market today.

In fact, within 1 to 2 years after treatment, most men with intact nerves will see a substantial improvement. However, modern studies have shown that overall about 40% of men lose erectile function after surgery. The skill of your surgeon or physician can have a significant impact on this outcome, so it is very important to select your team carefully. Men with baseline erectile dysfunction and/or other conditions that impair the ability to maintain an erection, such as diabetes or vascular problems, will have a more difficult time returning to pre-treatment function. It's important to remember that your maximum functionality after treatment can only be as good as it was before treatment.

## Four main components of erectile function may be affected by prostate cancer treatment:

- 1. Libido (sex drive) is most commonly affected by hormone therapy, or treatment that decreases your testosterone. You can have a low libido and still obtain an erection, but it is usually more difficult for men who have less interest in sex. This will return once your testosterone returns to normal after completing hormone therapy. Diagnosis and treatment can bring about complex feelings that include sadness, anger, and anxiety. These are normal feelings that, when unmanaged, can likewise compromise your sex drive; don't be shy about seeking individual or couples counseling during treatment.
- Mechanical ability is the ability to achieve a firm erection. It is controlled by the nerves and vessels that are intimately associated with the prostate and structures near the penis. Mechanical ability is most affected by surgery or radiation therapy.
- 3. Orgasm/climax can be more difficult after treatment, especially if libido is low or your erections are not as firm as they used to be. Also, sometimes there can be some discomfort initially after treatment when you climax. This usually is transient and will resolve. It is important to distinguish orgasm from ejaculation, as men will

- continue to have the pleasure sensation of orgasm without ejaculation.
- 4. The quantity of ejaculate may be minimal after treatment. The prostate and seminal vesicles which function to produce ejaculate are removed and/ or irradiated during treatment, so it is common to have minimal or no ejaculate afterwards. So although you may be able to have an erection and reach an orgasm, nothing may come out.

#### Considerations in surgery and radiation therapy

Prostatectomy: Since the 1980s, most men with localized disease are treated with what is termed a "nerve-sparing" prostatectomy. The goal of the procedure is to take the prostate and seminal vesicles out while sparing the nerves adjacent to the prostate. Studies have shown that approximately 50-60% of men who have the ability to have an erection before surgery will maintain this ability long-term. This number varies tremendously with surgeon expertise, and can increase or decrease based on age, obesity, and the ability to spare the nerves, which is related to the extent of disease. If you receive radiation therapy after surgery, your likelihood of erectile dysfunction will increase, since you are being exposed to the cumulative side effects of both treatments.

Radiation therapy: Similar to surgery, damage to blood vessels and nerves after radiation therapy can result in decreased erectile function over time. In general, radiation therapy has less of an impact on erectile function in the first 5 to 10 years after treatment compared with surgery, and approximately 70% of men who have baseline erectile function before treatment will keep erectile function after treatment. However, radiation therapy has a slower delay in erectile function decline than surgery; within 15 years after treatment, the rates are similar to those who underwent surgery.

In the long run, these rates do not appear to be affected by the use of short-term (4 to 6 months) hormone therapy, but may be affected by the use of long-term (18 to 36 months) hormone therapy.

Newer techniques in radiation therapy, termed "vessel-sparing" radiation therapy, have shown promising results for improving the preservation of erectile function, with close to 80% of men maintaining

#### Management of Erectile Dysfunction

There are many ways to help men who are experiencing ED. Below is a brief summary; for more information, go to pcf.org/guides to download the Prostate Cancer Patient Guide. Consult your doctor about which of these may be right for you, and be sure to discuss any other health problems that might influence your choice.

- ➤ Oral medications such as sildenafil (Viagra®) relax the arteries in the penis, allowing blood to rapidly flow in. About 75% of men who undergo nerve-sparing prostatectomy or more precise forms of radiation therapy have reported successfully achieving erections after using these drugs.
- ▶ Alprostadil (MUSE®) is a tiny medicated pellet that is inserted into the opening at the tip of the penis. It also stimulates blood flow into the penis. About 40% of men have reported successfully achieving erections after using this drug, though the results are inconsistent.
- ▶ Alprostadil (CaverJect®) uses the same drug that is in the MUSE pellets delivered via an injection directly into the penis. Although nearly 90% of men using CaverJect reported having erections, many men have a concern about injecting themselves regularly. However, it is one of the most consistently effective options after prostate cancer treatment.
- ➤ Mechanical devices, such as a vacuum pump, may be a solution for those unwilling or unable to use any form of medication to help improve erectile function, or as an adjunct to medications. About 80% of men find this device successful, but it, too, has a high drop-out rate.
- ➤ A surgically inserted penile implant can be up to 100% effective, and about 90% of men remain satisfied with their implants even after 10 years. The implant consists of a narrow, flexible plastic tube, a small balloon-like structure and a release button.

baseline function. This technique is being tested in an ongoing randomized trial. Ask your radiation oncologist about vessel-sparing radiation therapy.

#### Side Effects from Treatments for Advanced Prostate Cancer

This section discusses the side effects of common therapies used to treat patients with advanced prostate cancer: hormone therapy and chemotherapy. Early management of side effects has been shown to help patients live longer, better lives. Communicate with your doctor as soon as you experience any side effect of treatment.

#### Side Effects of Hormone Therapy

Testosterone is the primary male hormone, and plays an important role in establishing and maintaining typical male characteristics. The primary systemic treatment for prostate cancer, androgen deprivation therapy (ADT), lowers testosterone and causes side effects related to reversing all of the normal functions of testosterone.

Although most men may experience only a few of these symptoms, the list of potential effects of testosterone loss is long: hot flashes, decreased sexual desire, loss of bone density and increased fracture risk (osteoporosis), erectile dysfunction, fatigue, increased risk of diabetes and heart attacks, weight gain, decreased muscle mass, anemia, and memory loss.

At this time, it is not possible to predict how severely any individual will be affected by lowering testosterone with hormone therapy, but work is being done to find ways to help predict who might be affected by which effects.

Changes in diet and exercise have been shown to relieve many of the side effects of ADT. Before beginning hormone therapy, every man should discuss the effects of testosterone loss with his doctor and nutritionist, so he can alter his lifestyle to accommodate or head off the changes, as well as to ensure that he is monitored for changes in bone density and cholesterol.

#### Side Effects of 2nd-Generation Hormone Therapy

The newer anti-androgen drugs (abiraterone, apalutamide, enzalutamide, and, most recently, darolutamide) are used when prostate cancer has become resistant to traditional ADT, and, increasingly, earlier in the management of advanced disease. They each have their own side effect profile. You and your doctor will need to consider your disease status and other medical conditions in choosing among these agents.

#### Side Effects of Chemotherapy

Chemotherapy drugs are powerful and can take a toll on the body. Reactions to drugs can vary widely from patient to patient, so it's important to pay attention to any side effects that you experience, expected or otherwise.

The chemotherapy drug docetaxel is well tolerated, and many men are surprised to find that disease-related symptoms (pain, fatigue, loss of energy) are improved after starting this therapy. Side effects include fever and low white blood cell count, significant fatigue (especially in the first week of each cycle), and neuropathy (numbness or weakness in the fingers and/or toes). Cabazitaxel affects blood cell count and is almost always given with the medication Neulasta® to boost infection-fighting white blood cells, because life-threatening infection due to a depressed immune system is the most serious side effect associated with this medication. Blood transfusions are sometimes necessary to treat anemia caused by a low number of red blood cells.

Regardless of the type of chemotherapy you are receiving, you will be monitored very closely by doctors, nurses, and pharmacists to make sure that all side effects are being addressed. Many of these side effects, especially fever and inability to keep food/drink down, need to be addressed right away – don't wait until your next appointment to tell your provider.

