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Treating Cervical Cancer

If you've been diagnosed with cervical cancer, your cancer care team will talk with you about treatment options. In choosing your treatment plan, you and your cancer care team will also take into account your age, your overall health, and your personal preferences.

How is cervical cancer treated?

Common types of treatments for cervical cancer include:

- Surgery for Cervical Cancer
- Radiation Therapy for Cervical Cancer
- Chemotherapy for Cervical Cancer
- Targeted Drug Therapy for Cervical Cancer
- Immunotherapy for Cervical Cancer

Common treatment approaches

Depending on the type and stage of your cancer, you may need more than one type of treatment. For the earliest stages of cervical cancer, either surgery or radiation combined with chemo may be used. For later stages, radiation combined with chemo is usually the main treatment. Chemo (by itself) is often used to treat advanced cervical cancer.

Treatment Options for Cervical Cancer, by Stage

Who treats cervical cancer?

Doctors on your cancer treatment team may include:

- A gynecologist: a doctor who treats diseases of the female reproductive system
- A gynecologic oncologist: a doctor who specializes in cancers of the female reproductive system who can perform surgery and prescribe chemotherapy and other medicines
- A radiation oncologist: a doctor who uses radiation to treat cancer
- A medical oncologist: a doctor who uses chemotherapy and other medicines to treat cancer

Many other specialists may be involved in your care as well, including nurse practitioners, nurses, psychologists, social workers, rehabilitation specialists, and other health professionals.

• Health Professionals Associated with Cancer Care

Making treatment decisions

It's important to discuss all of your treatment options, including their goals and possible side effects, with your doctors to help make the decisions that best fit your needs. It's also very important to ask questions if there's anything you're not sure about. Although the choice of treatment depends largely on the stage of the disease at the time of diagnosis, other factors that may influence your options are your age, your general health, your individual circumstances, and your preferences. Cervical cancer can affect your sex life and your ability to have children. These concerns should also be considered as you make treatment decisions. Be sure that you understand all the risks and side effects of the various treatments before making a decision.

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 Cervical Cancer
- Fertility and Sexual Side Effects
- Seeking a Second Opinion

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.

Surgery for Cervical Cancer

- Surgery for cervical pre-cancers
- Surgery for invasive cervical cancer
- Surgery to remove nearby lymph nodes
- More information about Surgery

Many women with cervical cancer will have some type of surgery. Surgery can be used to:

- Help diagnose cervical cancer
- Help determine how far the cancer has spread
- Help treat the cancer (especially for early-stage cancers)

Surgery for cervical pre-cancers

Two types of procedures can be used to treat pre-cancers of the cervix:

- Ablation destroys cervical tissue with cold temperatures or with a laser rather than removing it.
- Excisional surgery (conization) cuts out and removes the pre-cancer.

Cryosurgery

Cryosurgery is a type of ablation where a very cold metal probe is placed directly on the cervix. This kills the abnormal cells by freezing them. It is used to treat cervical intraepithelial neoplasia (CIN). This can be done in a doctor's office or clinic. After cryosurgery, you may have a watery brown discharge for a few weeks.

Laser ablation

Laser ablation directs a focused laser beam through the vagina to vaporize (burn off) abnormal cells. This might be done in a doctor's office under local anesthesia (numbing medicine) or in the operating room with general anesthesia since it can cause more discomfort than cryotherapy. It is also used to treat cervical intraepithelial neoplasia (CIN).

Conization

Another way to treat cervical intraepithelial neoplasia (CIN) is with excisional surgery called conization. The doctor removes a cone-shaped piece of tissue from the cervix. The tissue removed in the cone includes the transformation zone where cervical precancers and cancers are most likely to start. A cone biopsy is not only used to diagnose pre-cancers and cancers. It can also be used as a treatment since it can sometimes completely remove pre-cancers and some very early cancers.

The procedure can be done in different ways:

- Using a surgical blade (cold knife cone biopsy)
- Using a laser beam (laser conization)
- Using a thin wire heated by electricity (the <u>loop electrosurgical excision procedure</u>, LEEP or LEETZ procedure).

Surgery for invasive cervical cancer

Procedures to treat invasive cervical cancer are:

- Hysterectomy (simple or radical)
- Trachelectomy

Simple hysterectomy

A simple hysterectomy removes the uterus (both the body of the uterus and the cervix) but not the structures next to the uterus (parametria and uterosacral ligaments). The vagina and pelvic lymph nodes are not removed. The ovaries are usually left in place unless there is another reason to remove them.

Simple hysterectomy can be used to treat certain types of severe CIN or certain types of very early cervical cancer.

There are different ways to do a hysterectomy:

- **Abdominal hysterectomy:** The uterus is removed through a surgical incision in the front of the abdomen.
- Vaginal hysterectomy: The uterus is removed through the vagina.
- Laparoscopic hysterectomy: The uterus is removed using laparoscopy. First, a thin tube with a tiny video camera at the end (the laparoscope) is inserted into one or more very small surgical incisions made on the abdominal wall to see inside the abdomen and pelvis. Small instruments can be controlled through the tube(s), so the surgeon can cut around the uterus without making a large cut in the abdomen. The uterus is then removed through a cut in the vagina.
- Robotic-assisted surgery: In this approach, the laparoscopy is done with special tools attached to robotic arms that are controlled by the doctor to help perform

precise surgery.

General anesthesia is used for all of these operations.

For a laparoscopic or vaginal hysterectomy, the hospital stay is usually 1 to 2 days, followed by a 2- to 3-week recovery period. A hospital stay of 3 to 5 days is common for an abdominal hysterectomy, and complete recovery takes about 4 to 6 weeks.

Possible side effects: Any type of hysterectomy results in infertility (inability to have children). Complications are unusual but could include bleeding, infection, or damage to the urinary or intestinal systems such as the bladder or colon.

Hysterectomy does not change a woman's ability to feel sexual pleasure. A woman does not need a uterus or cervix to reach orgasm. The area around the clitoris and the lining of the vagina remain as sensitive as before a hysterectomy. More information about managing the sexual side effects of cervical cancer treatment can be found in Sex and the Woman with Cancer.¹

Radical hysterectomy

For this operation, the surgeon removes the uterus along with the tissues next to the uterus (the parametria and the uterosacral ligaments), the cervix, and the upper part (about 1 inch [2-3cm]) of the vagina next to the cervix. The ovaries are not removed unless there is some other medical reason to do so. More tissue is removed in a radical hysterectomy than in a simple one, so the hospital stay can be longer. Some lymph nodes will also be removed and checked for cancer at this time.

This surgery is usually done through a large abdominal incision (also known as open surgery). Often, some pelvic lymph nodes are removed as well. (This procedure, known as **lymph node dissection**, is discussed later in this section.)

A radical hysterectomy can also be done using laparoscopy or robot-assistance. (See the Simple hysterectomy section for a description of laparoscopy.) These techniques are also referred to as minimally invasive surgery. Laparoscopic (or robotic) surgery can result in less pain, less blood loss during the operation, and a shorter hospital stay compared to open surgery. However, it is very important to note that recent studies have shown that women who have minimally invasive radical hysterectomies for cervical cancer have a higher chance of the cancer recurring and a higher risk of dying from the cancer than those who have surgery through an abdominal incision (open surgery). Having a radical hysterectomy through an abdominal cut is the preferred type of surgery in most cases. Laparoscopic surgery may still be an option for a small

specific group of women with early stage cancer, but you should discuss your options carefully with your doctor.

A **modified radical hysterectomy** is similar to a radical hysterectomy but does not remove as much of the vagina and tissues next to the uterus (the parametria and the uterosacral ligaments) and lymph nodes are usually not removed.

Possible side effects: Because the uterus is removed, this surgery results in infertility. Because some of the nerves to the bladder are removed, some women have problems emptying their bladder after this operation and may need a catheter for a time. Complications are unusual but could include bleeding, infection, or damage to the urinary and intestinal systems such as the bladder or colon.

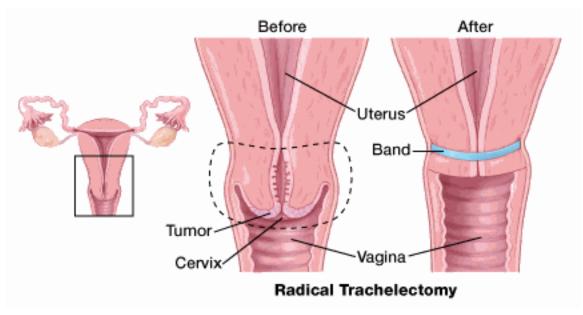
Removal of some of the lymph nodes to check for cancer may sometimes result in lymphedema² (leg swelling). This is not common, but may happen after surgery and treated with different methods.

Radical hysterectomy does not change a woman's ability to feel sexual pleasure. Although the vagina is shortened, the area around the clitoris and the lining of the vagina is as sensitive as before. A woman does not need a uterus or cervix to reach orgasm. When cancer has caused pain or bleeding with intercourse, the hysterectomy may actually improve a woman's sex life by stopping these symptoms. More information about managing the sexual side effects of cervical cancer treatment can be found in Sex and the Woman with Cancer³.

Trachelectomy

A **radical trachelectomy**, allows women to be treated without losing their ability to have children. The operation is done either through the vagina or the abdomen, and is sometimes done using laparoscopy.

This procedure removes the cervix and the upper part of the vagina but not the body of the uterus. The surgeon then places a permanent "purse-string" stitch inside the uterine cavity to keep the opening of the uterus closed, the way the cervix normally would.



The nearby lymph nodes are also removed using laparoscopy which may require another incision (cut). The operation is done either through the vagina or the abdomen.

After trachelectomy, some women are able to carry a pregnancy to term and deliver a healthy baby by cesarean section, although women who have had this surgery might have a higher risk of miscarriage.

Pelvic exenteration

This operation is done for very specific cases of recurrent cervical cancer. In this surgery, all of the same organs and tissues are removed as in a radical hysterectomy with pelvic lymph node dissection. (Lymph node dissection is discussed in the next section.) In addition, the bladder, vagina, rectum, and part of the colon is also removed, depending on where the cancer has spread.

If your bladder is removed, you will need a new way to store and get rid of urine. This usually means using a short piece of intestine to function as a new bladder. The new bladder may be connected to the abdominal wall so that urine is drained periodically when the patient places a catheter into a urostomy (a small opening). Or urine drains continuously into a small plastic bag attached to the front of the abdomen. For more information, see Urostomy Guide⁴.

If the rectum and part of the colon are removed, a new way to get rid of solid waste must be created. This is done by attaching the remaining intestine to the abdominal wall so that fecal material can pass through a small opening (stoma) into a small plastic bag worn on the front of the abdomen (more information about colostomies can be found

in <u>Colostomy Guide</u>⁵). In some cases, it may be possible to remove the cancerous part of the colon (next to the cervix) and reconnect the colon ends so that no bags or external appliances are needed.

If the vagina is removed, a new vagina can be surgically made out of skin, intestinal tissue, or muscle and skin (myocutaneous) grafts.

Sexual impact of pelvic exenteration

Recovery from total pelvic exenteration takes a long time. Most women don't begin to feel like themselves again for about 6 months after surgery. Some say it takes a year or two to adjust completely.

Nevertheless, these women can lead happy and productive lives. With practice, they can also have sexual desire, pleasure, and orgasms.

More information about managing the sexual side effects of cervical cancer treatment can be found in Sex and the Woman with Cancer⁶.

Surgery to remove nearby lymph nodes

Para-aortic lymph node sampling

Usually during surgery for a radical hysterectomy, the lymph nodes next to the aorta (the large artery in the abdomen) are removed. This is called **para-aortic lymph node sampling.** The lymph nodes may be sent to the lab during the operation for quick testing. If the para-aortic lymph nodes show cancer, the surgery may be stopped, and radiation and chemotherapy given instead. If the lymph nodes do not show cancer, then pelvic lymph nodes (see below) are usually removed and the radical hysterectomy completed. Any tissue removed during surgery will be tested to see if the cancer has spread there. If so, radiation therapy with or without chemotherapy might be recommended.

Pelvic lymph node dissection

Cancer that starts in the cervix can spread to lymph nodes (pea-sized collections of immune system cells) in the pelvis. To check for lymph node spread, the surgeon might remove some of these lymph nodes. This procedure is known as a **pelvic lymph node dissection** or **lymph node sampling**. It is done at the same time as a hysterectomy or trachelectomy.

Removing lymph nodes can lead to fluid drainage problems in the legs. This can cause severe leg swelling, a condition called <u>Lymphedema</u>⁷.

Sentinel lymph node mapping and biopsy

Sentinel lymph node mapping and biopsy is a procedure in which the surgeon finds and removes only the lymph node(s) where the cancer would likely spread first. To do this, the surgeon injects a radioactive substance and/or a blue dye into the cervix at the beginning of the surgery. Lymphatic vessels will carry these substances along the same path that the cancer would likely take. The first lymph node(s) the dye or radioactive substance travels to will be the sentinel node(s). Removing only one or a few lymph nodes lowers the risk of side effects from the surgery, such as leg swelling that is also known as lymphedema8.

After the substance has been injected, the sentinel node(s) can be found either by using a special machine to detect radioactivity in the nodes, or by looking for nodes that have turned blue. To double check, both methods are often used. The surgeon then removes the node(s) containing the dye or radioactivity.

Sentinel lymph node mapping may be considered for certain cases of stage I cervical cancer. It is best used for tumors that are less than 2 cm in size. If your surgeon is planning sentinel lymph node biopsies, you should discuss if this procedure is appropriate for you.

Even if sentinel lymph node mapping does not show any lymph nodes to biopsy, the surgeon will most likely still remove the lymph nodes on that side of the pelvis to make sure cancer is not missed. Also, any enlarged or suspicious lymph nodes need to be removed at the time of surgery, even if they do not map with dye.

More information about Surgery

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

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

Hyperlinks

- 1. <u>www.cancer.org/cancer/managing-cancer/side-effects/fertility-and-sexual-side-effects/sexuality-for-women-with-cancer.html</u>
- 2. www.cancer.org/cancer/managing-cancer/side-effects/swelling/lymphedema.html
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- 5. <u>www.cancer.org/cancer/managing-cancer/treatment-types/surgery/ostomies/colostomy.html</u>
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- 7. www.cancer.org/cancer/managing-cancer/side-effects/swelling/lymphedema.html
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Radiation Therapy for Cervical Cancer

- External beam radiation
- Long-term side effects of radiation therapy
- More information about radiation therapy

Radiation therapy uses high energy x-rays to kill cancer cells. Depending on the stage of the cervical cancer, radiation therapy may be used:

• As a part of the main treatment. For some stages of cervical cancer, the

preferred treatment is radiation alone or surgery followed by radiation. For other stages, radiation and chemo given together (called **concurrent chemoradiation**) is the preferred treatment as the chemo helps the radiation work better.

 To treat cervical cancer that has spread or that has come back after treatment. Radiation therapy may be used to treat cervical cancers that have spread to other organs and tissues.

The types of radiation therapy most often used to treat cervical cancer are:

- External beam radiation
- Brachytherapy

It is important to know that smoking increases the side effects from radiation and can make treatment less effective. If you smoke, you should stop.

External beam radiation

<u>External beam radiation therapy</u>¹ (EBRT) aims x-rays at the cancer from a machine outside the body. Treatment is much like getting a regular x-ray, but the radiation dose is stronger.

Each radiation treatment lasts only a few minutes, but getting you into place for treatment usually takes longer. The procedure itself is painless.

When EBRT is used as the main treatment for cervical cancer, it is usually combined with chemotherapy (called **concurrent chemoradiation**). Often, a low dose of the chemo drug called cisplatin is used. Other chemo drugs can be used as well. The radiation treatments are given 5 days a week for about 5 weeks. The chemotherapy is given at scheduled times during the radiation. The schedule is determined by which drug is used. If the cancer has not spread to distant areas, brachytherapy, which is discussed below, may also be given after the concurrent chemoradiation is complete.

EBRT can also be used as the main treatment of cervical cancer in patients who can't tolerate chemoradiation, can't safely have surgery, or choose not to have surgery. It can also be used by itself to treat areas of cancer spread.

Possible side effects of EBRT

Short-term side effects² of external beam radiation therapy for cervical cancer can

include:

- Fatigue (tiredness)
- Upset stomach
- Diarrhea or loose stools (if radiation is given to the pelvis or abdomen)
- Nausea and vomiting
- Skin changes (mild redness to peeling or flaking)
- Radiation cystitis: Radiation to the pelvis can irritate the bladder (radiation cystitis), causing discomfort, an urge to urinate often, and sometimes blood in the urine.
- **Vaginal pain:** Radiation can make the vulva and vagina more sensitive and sore, and sometimes causes a discharge.
- **Menstrual changes:** Pelvic radiation can affect the ovaries, leading to menstrual changes and even early menopause
- Low blood counts: Anemia (low levels of red blood cells) can make you feel tired.
 Neutropenia (low levels of white blood cells) increases the risks of serious infection.
 Thrombocytopenia (low levels of platelet counts) increases the risk of bleeding.

When chemotherapy is given with radiation, the blood counts tend to be lower and fatigue and nausea tend to be worse. These side effects typically improve in the weeks after treatment is stopped.

Other, long-term side effects are also possible with EBRT. These are described below.

Brachytherapy (internal radiation therapy)

<u>Brachytherapy</u>³, or internal radiation therapy, puts a source of radiation in or near the cancer. This type of radiation only travels a short distance. The type of brachytherapy used most often to treat cervical cancer is known as **intracavitary brachytherapy**. The radiation source is placed in a device in the vagina (and sometimes in the cervix). Brachytherapy is mainly used in addition to EBRT as a part of the main treatment for cervical cancer. Rarely, it might be used alone in very specific cases of early-stage cervical cancers.

There are two types of brachytherapy:

• Low-dose rate (LDR) brachytherapy is completed over a few days. During this time, the patient stays in bed in a private room in the hospital with instruments

holding the radioactive material in place. While the radiation therapy is being given, the hospital staff will care for you, but will also take precautions to avoid being exposed to radiation themselves.

 High-dose rate (HDR) brachytherapy is done as an outpatient over several treatments (often at least a week apart). For each high-dose treatment, the radioactive material is inserted for a few minutes and then removed. The advantage of HDR treatment is that you do not have to stay in the hospital or stay still for long periods of time.

To treat cervical cancer in women who have had a hysterectomy, the radioactive material is placed in a tube in the vagina.

To treat a woman who still has a uterus, the radioactive material can be placed in a small metal tube (called a **tandem**)that goes in the uterus, along with small round metal holders (**ovoids**) placed near the cervix. This is sometimes called tandem and ovoid treatment.

Another option is called tandem and ring. For this, a round holder (like a disc) is placed close to the uterus. The choice of which one to use depends on what type of brachytherapy is planned.

Possible short-term side effects of brachytherapy

Since the radiation only travels a short distance with brachytherapy, the main effects of the radiation are on the cervix and the walls of the vagina. The most common side effect is irritation of the vagina. It may become red and sore, and there may be a discharge. The vulva may become irritated as well.

Brachytherapy can also cause many of the same <u>side effects</u>⁴as EBRT, such as fatigue, diarrhea, nausea, irritation of the bladder, and low blood counts. Often brachytherapy is given right after external beam radiation (before the side effects can go away), so it can be hard to know which type of treatment is causing the side effect.

Long-term side effects of radiation therapy

Women can experience side effects related to radiation months to years after treatment.

Vaginal stenosis: Both EBRT and brachytherapy can cause scar tissue to form in the vagina. The scar tissue can make the vagina narrower (called vaginal stenosis), less able to stretch, or even shorter, which can make vaginal sex painful.

A woman can help prevent this problem by stretching the walls of her vagina several times a week, either by having sex or by using a vaginal dilator (a plastic or rubber tube used to stretch out the vagina). For more information, see <u>Sex and the Women With Cancer⁵</u>.

Vaginal dryness: Vaginal dryness and painful sex can be long-term side effects from radiation (both brachytherapy and EBRT). Estrogens used locally may help with vaginal dryness and changes to the vaginal lining, especially if radiation to the pelvis damaged the ovaries, and caused early menopause. These hormones are typically applied in the vagina and absorbed into the genital area, rather than taken by mouth. They come in gel, cream, ring, and tablet forms. For more information, see <u>Sex and the Women With Cancer⁶</u>.

Rectal bleeding/rectal stenosis: Radiation to the rectal wall can cause chronic inflammation of the area which can lead to bleeding and sometimes stenosis (narrowing) of the rectum which can be painful. An abnormal opening (called a fistula) also may form between the rectum and vagina, causing stool to come out of the vagina. These problems typically happen during the first 3 years after radiation treatment. Additional treatments, such as surgery, may be needed to fix these complications.

Urinary problems: Radiation to the pelvis can cause chronic radiation cystitis (as mentioned above), blood in the urine, or an abnormal opening between the bladder and vagina (called a fistula). These side effects can be seen many years after radiation therapy.

Weakened bones: Radiation to the pelvis can weaken the bones, leading to fractures. Hip fractures are the most common, and might occur 2 to 4 years after radiation. Bone density tests are recommended to monitor the risk of fracture.

Swelling of the leg(s): If pelvic lymph nodes are treated with radiation, it can lead to fluid drainage problems in the leg. This can cause the leg to swell severely, a condition calledlymphedema⁷.

If you are having side effects from radiation treatment, discuss them with your cancer care team.

More information about radiation therapy

To learn more about how radiation is used to treat cancer, see Radiation Therapy⁸.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>⁹.

Hyperlinks

- 1. <u>www.cancer.org/cancer/managing-cancer/treatment-types/radiation/external-beam-radiation-therapy.html</u>
- 2. www.cancer.org/cancer/managing-cancer/side-effects.html
- 3. <u>www.cancer.org/cancer/managing-cancer/treatment-types/radiation/internal-radiation-therapy-brachytherapy.html</u>
- 4. <u>www.cancer.org/cancer/managing-cancer/treatment-types/radiation/effects-on-different-parts-of-body.html</u>
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- 6. <u>www.cancer.org/cancer/managing-cancer/side-effects/fertility-and-sexual-side-effects/sexuality-for-women-with-cancer.html</u>
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Chemotherapy for Cervical Cancer

- As part of the main treatment for cervical cancer
- For cervical cancer that has spread or come back after treatment
- How is chemotherapy given?
- Side effects of chemotherapy for cervical cancer
- More information about chemotherapy

Chemotherapy (chemo) uses anti-cancer drugs that are injected into a vein or given by mouth. These drugs enter the bloodstream and can reach almost all areas of the body, making this treatment useful for killing cancer cells in most parts of the body.

Not all women with cervical cancer will need chemo, but there are a few situations in which chemo may be recommended:

As part of the main treatment for cervical cancer

For some stages of cervical cancer, the preferred treatment is <u>radiation</u> and chemo given together (called **concurrent chemoradiation**). The chemo helps the radiation work better. Options for concurrent chemoradiation include:

- Cisplatin given weekly during radiation. This drug is given into a vein (IV) before the radiation appointment. (If cisplatin is not a good option, carboplatin may be used instead.)
- Cisplatin plus 5-fluorouracil (5-FU) given every 3 weeks during radiation.

For cervical cancer that has spread or come back after treatment

Chemo may be used to treat cervical cancer that has spread to other organs and tissues (advanced cervical cancer). It can also be helpful when cervical cancer comes back after treatment with chemoradiation (recurrent cervical cancer).

The chemo drugs most often used to treat cervical cancer that has come back or spread to other areas include:

- Cisplatin
- Carboplatin

- Paclitaxel (Taxol)
- Topotecan

Combinations of these drugs are often used.

Some other drugs can be used as well, such as docetaxel (Taxotere), ifosfamide (Ifex), 5-fluorouracil (5-FU), irinotecan (Camptosar), gemcitabine (Gemzar)and mitomycin.

Bevacizumab (Avastin), a targeted drug, may be added to chemo.

How is chemotherapy given?

Chemo drugs for cervical cancer are typically given into a vein (IV), either as an injection over a few minutes or as an infusion in a vein over a longer period of time. This can be done in a doctor's office, infusion center, or in a hospital setting.

Chemo is given in cycles, followed by a rest period to give you time to recover from the effects of the drugs. Cycles are most often weekly 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.

Sometimes, a slightly larger and sturdier IV is required to give chemo. These are known as <u>central venous catheters</u>¹ (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 blood for testing.

There are many different kinds of central venous catheters (CVCs). The most common types are the port and the PICC line.

Side effects of chemotherapy for cervical cancer

Chemo drugs kill cancer cells but also damage some normal cells, which can lead to certain <u>side effects</u>². Side effects depend on the type and dose of the drugs and the length of time you are treated. Many side effects are short-term and go away after treatment is finished, but some can last a long time or even be permanent. It's important to tell your health care team if you have any side effects, as there are often ways to lessen them.

Common short term side effects of chemotherapy can include:

- Nausea and vomiting
- Loss of appetite
- Hair loss
- Mouth sores
- Fatigue (tiredness)

Because chemotherapy can damage the blood-producing cells of the bone marrow, the blood cell counts might become low³. This can result in:

- An increased chance of infection from a shortage of white blood cells (called neutropenia)
- Bleeding or bruising after minor cuts or injuries because of a shortage of blood platelets (called thrombocytopenia)
- Shortness of breath or fatigue due to low red blood cell counts (called anemia)

When chemo is given with radiation, the side effects are often more severe. The nausea, fatigue, diarrhea, and problems with low blood counts are often worse.

Your health care team will watch for side effects and can give you medicines to help prevent them or treat them to help you feel better. For example, you can be given drugs to help prevent or reduce nausea and vomiting.

Long-term side effects of chemotherapy can include:

Menstrual changes: For younger women who have not had their uterus removed as a part of treatment, changes in menstrual periods are a common side effect of chemo. But even if your periods stop while you are on chemo, you might still be able to get pregnant. Getting pregnant while receiving chemo is not safe, as it could lead to birth defects and interfere with treatment. This is why it's important that women who are premenopausal before treatment and are sexually active discuss with their doctor the options for birth control. Patients who have finished treatment (like chemo) can often go on to have children, but it's important to talk to your doctor about when it is safe to do so.

Premature menopause (not having any more menstrual periods) and infertility (not being able to become pregnant) may occur and may be permanent. Some chemo drugs are more likely to cause this than others. The older a woman is when she gets chemo, the more likely it is that she will become infertile or go through menopause as a result. If this happens, there is an increased risk of bone loss and osteoporosis. Medicines that can treat or help prevent problems with bone loss are available.

Neuropathy: Some drugs used to treat cervical cancer, including paclitaxel and cisplatin, can <u>damage nerves</u>⁴ outside of the brain and spinal cord. The injury can sometimes lead to symptoms like numbness, pain, burning or tingling sensations, sensitivity to cold or heat, or weakness, mainly in the hands and feet. This called <u>peripheral neuropathy</u>⁵. In most cases this gets better or even goes away once treatment stops, but it might last a long time in some women.

Nephrotoxicity: Cisplatin, the main chemo drug used to treat cervical cancer, can damage the kidneys (also called nephrotoxicity). Many times the damage is preventable and reversible, but sometimes the damage may be long-lasting. Often, there are no symptoms, but the damage can be seen on bloodwork done routinely while chemo is given. If kidney damage happens, the cisplatin is usually stopped and carboplatin may be used instead.

Other side effects are also possible. Some of these are more common with certain chemo drugs. Ask your cancer care team to tell you about the possible side effects of the specific drugs you are getting.

More information about chemotherapy

For more general information about how chemotherapy is used to treat cancer, see Chemotherapy⁶.

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects⁷.

Hyperlinks

- 1. www.cancer.org/cancer/managing-cancer/making-treatment-decisions/tubes-lines-ports-catheters.html
- 2. www.cancer.org/cancer/managing-cancer/side-effects.html
- 3. www.cancer.org/cancer/managing-cancer/side-effects/low-blood-counts.html
- 4. <u>www.cancer.org/cancer/managing-cancer/side-effects/nervous-system/peripheral-neuropathy.html</u>
- 5. <u>www.cancer.org/cancer/managing-cancer/side-effects/nervous-system/peripheral-neuropathy.html</u>
- 6. www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html
- 7. www.cancer.org/cancer/managing-cancer/side-effects.html

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Targeted Drug Therapy for Cervical Cancer

- Drugs that target blood vessel formation
- Antibody-drug conjugates
- More information about targeted therapy

Targeted drug therapy is the use of medicines that target or are directed at proteins on cervical cancer cells that help them grow, spread, or live longer. Targeted drugs work to destroy cancer cells or slow down their growth. They have different side effects than chemotherapy and some are taken as a pill.

Some targeted therapy drugs, for example, monoclonal antibodies, work in more than

one way to control cancer cells and may also be considered immunotherapy because they boost the immune system.

Different types of targeted drug therapy can be used to treat cervical cancer.

Drugs that target blood vessel formation

Vascular endothelial growth factor (VEGF) is a protein that helps tumors form new blood vessels (a process known as **angiogenesis**) to get nutrients they need to grow. Some targeted drugs called **angiogenesis inhibitors** stop VEGF from working and block this new blood vessel growth.

Bevacizumab (Avastin®) is an angiogenesis inhibitor that can be used to treat advanced cervical cancer. It is a monoclonal antibody (a man-made version of a specific immune system protein) that targets VEGF.

This drug is often used with chemo for a time. Then, if the cancer responds, the chemo may be stopped and the bevacizumab given by itself until the cancer starts growing again.

Possible side effects of drugs that target VEGF

The possible side effects of this drug are different from those of chemotherapy drugs. Some of the more common side effects can include:

- High blood pressure
- · Feeling tired
- Nausea

Less common but more serious side effects can include:

- Problems with bleeding
- Blood clots
- Wound healing
- Heart failure or a heart attack

Other rare but serious side effects are the formation of an abnormal opening (called a **fistula**) between the vagina and part of the colon or intestine or the formation of a hole in the bowel.

Antibody-drug conjugates

An antibody-drug conjugate (ADC) is a monoclonal antibody linked to a chemotherapy drug.

Tisotumab vedotin-tftv (Tivdak): This ADC has an antibody that targets tissue-factor (TF) protein on cancer cells. It acts like a homing signal by attaching to the TF protein bringing the chemo directly to the cancer cell. It can be used to treat cervical cancer that has spread (metastasized) to another part of the body or come back after initial treatment (recurred), typically after at least 2 other drug treatments have been tried. This drug is given in a vein (IV).

Possible side effects of tisotumab vedotin-tftv

Common side effects can include feeling tired, nausea, hair loss, vomiting, bleeding, diarrhea, rash, and nerve damage (peripheral neuropathy).

Common lab abnormalities that might be seen with this drug include low red blood cell counts (anemia), low white blood cell counts, and abnormal kidney function.

This drug can have **major side effects involving the eyes**. People taking this drug can have dry eye, changes in vision, vision loss, or ulceration of the cornea. They should have regular eye exams while on this drug and tell their healthcare team right away if they have any eye symptoms.

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>¹.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>².

Hyperlinks

- 1. <u>www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html</u>
- 2. www.cancer.org/cancer/managing-cancer/side-effects.html

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Immunotherapy for Cervical Cancer

- Immune checkpoint inhibitors
- Possible side effects of immunotherapy
- More information about immunotherapy

Immunotherapy is the use of medicines to boost a person's own immune system to recognize and destroy cancer cells more effectively. Immunotherapy typically works on specific proteins involved in the immune system to enhance the immune response. They have different and sometimes less severe side effects than chemotherapy.

Some immunotherapy drugs, for example, monoclonal antibodies, work in more than one way to control cancer cells and may also be considered targeted therapy because they block a specific protein on the cancer cell to keep it from growing.

Immunotherapy can sometimes be used to treat cervical cancer.

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 "checkpoints" – proteins on immune cells that need to be turned on (or off) to start an immune response. Cancer cells sometimes use these checkpoints to avoid being attacked by the immune system. Newer drugs that target these checkpoints are being used as cancer treatments.

Pembrolizumab (Keytruda) targets PD-1, a protein on immune system cells called **T cells** that normally helps keep these cells from attacking other cells in the body. By blocking PD-1, these drugs boost the immune response against cancer cells. This can shrink some tumors or slow their growth.

Before pembrolizumab can be used, a lab test might need to be done on the cancer cells to show they have at least a certain amount of the PD-L1 protein.

If enough PD-L1 protein is detected, pembrolizumab can be used:

- By itself for cervical cancer that has come back or that has spread while getting chemotherapy or after chemotherapy.
- As a first treatment, along with chemotherapy, with or without bevacizumab, for cervical cancer that is not shrinking with current treatment, has come back, or has spread to distant sites.

This immunotherapy drug is given as an intravenous (IV) infusion every 3 or 6 weeks.

Possible side effects of immunotherapy

Side effects of immunotherapy drugs can include fatigue, fever, nausea, headache, skin rash, loss of appetite, constipation, joint/muscle pain, and diarrhea.

Other, more serious side effects occur less often. These drugs work by basically removing the brakes on the body's immune system. Sometimes the immune system starts attacking other parts of the body, which can cause serious or even life-threatening problems in the lungs, intestines, liver, hormone-making glands, kidneys, or other organs.

It's very important to report any new side effects to your health care team right away. If you do have a serious side effect, treatment may need to be stopped and you may be given 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 Cancer Immunotherapy¹.

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects².

Hyperlinks

- 1. www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html
- 2. www.cancer.org/cancer/managing-cancer/side-effects.html

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Treatment Options for Cervical Cancer,

by Stage

- Stage IA1
- Stage IA2
- Stages IB and IIA
- Stages IIB, III, IVA
- Stage IVB
- Cervical cancer in pregnancy

The stage of a cervical cancer is the most important factor in choosing treatment. But other factors can also affect your treatment options, including the exact location of the cancer within the cervix, the type of cancer (squamous cell or adenocarcinoma), your age and overall health, and whether you want to have children.

Stage IA1

Treatment for this stage depends on whether or not you want to be able to have children (maintain fertility) and whether or not the cancer has grown into blood or lymph vessels (called lymphovascular invasion).

Treatment options for women who want to maintain fertility

A **cone biopsy** is the preferred procedure for women who want to have children after the cancer is treated.

- If the edges of the cone don't contain cancer cells (called negative margins), the woman can be watched closely without further treatment as long as the cancer doesn't come back.
- If the edges of the cone biopsy have cancer cells (called positive margins), then cancer may have been left behind. This can be treated with a repeat cone biopsy or a radical trachelectomy.
- If the cancer has grown into blood or lymph vessels, one treatment option is a cone biopsy (with negative margins) with removal of pelvic lymph nodes. Another option is a radical trachelectomy along with removal of the pelvic lymph nodes.

Treatment options for women who don't want to maintain fertility

- A simple hysterectomy may be an option if the cancer shows no lymphovascular invasion and the edges of the biopsy have no cancer cells. If the edges of the biopsy have cancer cells present, a repeat cone biopsy or a radical hysterectomy with removal of the pelvic lymph nodes might be an option.
- If the cancer has grown into blood or lymph vessels, you might need a radical hysterectomy along with removal of the pelvic lymph nodes. Sometimes, surgery is not done and external beam radiation to the pelvis followed by brachytherapy is used.

If none of the lymph nodes are found to have cancer, radiation may still be discussed as an option if the tumor is large, if the tumor has grown into blood or lymph vessels, or if the tumor is invading the surrounding connective tissue that supports organs such as the uterus, bladder, vagina (the stroma).

If the cancer has spread to the tissues next to the uterus (called the parametria) or to any lymph nodes, or if the tissue removed has positive margins, radiation (EBRT) with chemotherapy is usually recommended. The doctor may also advise brachytherapy after the combined chemo and radiation are done.

Stage IA2

Treatment for this stage depends in part on whether or not you want to continue to be able to have children (maintain fertility).

Treatment options for women who want to maintain fertility

- Cone biopsy with removal of pelvic lymph nodes (pelvic lymph node dissection)
- Radical trachelectomy with pelvic lymph node dissection

Treatment options for women who don't want to maintain fertility

- External beam radiation therapy (EBRT) to the pelvis plus brachytherapy
- Radical hysterectomy with removal of pelvic lymph nodes

If none of the lymph nodes have cancer cells, radiation may still be an option if the tumor is large, if the tumor has grown into blood or lymph vessels, or if the tumor is invading the surrounding connective tissue that supports organs such as the uterus, bladder, vagina (the stroma).

If the cancer has spread to the tissues next to the uterus (called the **parametria**) or to any lymph nodes, or if the tissue removed has positive margins, radiation (EBRT) with chemotherapy is usually recommended. The doctor may also advise brachytherapy after the combined chemo and radiation are done.

Stages IB and IIA

Stages IB1 and IB2

Treatment options for women who want to maintain fertility

 Radical trachelectomy with pelvic lymph node dissection and sometimes removal of the para-aortic lymph nodes

Treatment options for women who don't want to maintain fertility

- Radical hysterectomy with removal of lymph nodes in the pelvis and sometimes lymph nodes from the para-aortic area. If none of the lymph nodes are found to have cancer, radiation may still be discussed as an option if the tumor is large, if the tumor has grown into blood or lymph vessels, or if the tumor is invading the surrounding connective tissue that supports organs such as the uterus, bladder, vagina (the stroma). If the cancer has spread to the tissues next to the uterus (called the parametria) or to any lymph nodes, or if the tissue removed has positive margins, radiation (EBRT) with chemotherapy is usually recommended. The doctor may also advise brachytherapy after the combined chemo and radiation are done.
- Radiation using both brachytherapy and external beam radiation therapy may be an option if a woman is not healthy enough for surgery or if she decides she does not want surgery. Chemotherapy (chemo) may be given with the radiation (concurrent chemoradiation).

Stage IIA1

Treatment options

• Radical hysterectomy with pelvic lymph node dissection and para-aortic lymph node sampling: If cancer cells are found in the removed lymph nodes, or in the

- edges of the tissue removed (positive margins), surgery may be followed by radiation therapy, which is often given with chemo (concurrent chemoradiation).
- Radiation with or without chemotherapy: The radiation therapy includes both external beam radiation and brachytherapy. The chemo may be cisplatin, carboplatin, or cisplatin plus fluorouracil.

Stages IB3 and IIA2

Treatment options

- Chemoradiation: The chemo may be cisplatin, carboplatin, or cisplatin plus fluorouracil. The radiation therapy includes both external beam radiation and brachytherapy.
- Radical hysterectomy with pelvic lymph node dissection and para-aortic lymph node sampling: If cancer cells are found in the removed lymph nodes, or in the edges of the tissue removed (positive margins), surgery may be followed by radiation therapy, which is often given with chemo (concurrent chemoradiation).
- Chemoradiation followed by a hysterectomy

Stages IIB, III, IVA

Treatment options

Chemoradiation: The chemo may be cisplatin, carboplatin, or cisplatin plus fluorouracil. The radiation therapy includes both external beam radiation and brachytherapy.

Stage IVB

At this stage, the cancer has spread out of the pelvis to other areas of the body. Stage IVB cervical cancer is not usually considered curable. Treatment options include radiation therapy with or without chemo to try to slow the growth of the cancer or help relieve symptoms. Most standard chemo regimens include a platinum drug (cisplatin or carboplatin) along with another drug such as paclitaxel (Taxol), gemcitabine (Gemzar), or topotecan. The targeted drug bevacizumab (Avastin) with chemo, immunotherapy alone with pembrolizumab (Keytruda), the targeted drug tisotumab vedotin-tftv (Tivdak), or pembrolizumab (Keytruda) with chemo (with or without bevacizumab [Avastin]), may also be options.

<u>Clinical trials</u>¹ are testing other combinations of chemo drugs, as well as some other experimental treatments.

Recurrent cervical cancer

Cancer that comes back after treatment is called **recurrent cancer**. Cancer can come back locally (in or near where it first started, such as the cervix, uterus or nearby the pelvic organs), or it can come back in distant areas (such as the lungs or bone).

If the cancer has recurred in the center of the pelvis only, extensive surgery (such as pelvic exenteration) may be an option for some patients, and offers the best chance for possibly curing the cancer (although it can have major side effects). Radiation therapy (sometimes along with chemo) might be another option. If not, chemo, immunotherapy, or targeted therapy may be used to slow the growth of the cancer or help relieve symptoms, but they aren't expected to cure the cancer.

No matter which type of treatment your doctor recommends, it's important that you understand the goal of treatment (to try to cure the cancer, control its growth, or relieve symptoms), as well as its possible side effects and limitations. For example, sometimes chemo can improve your quality of life, and other times it might diminish it. You need to discuss this with your doctor.

New treatments that may benefit patients who have distant recurrence of cervical cancer are being evaluated in <u>clinical trials</u>².

Cervical cancer in pregnancy

A small number of cervical cancers are found in pregnant women. Most of these (70%) are stage I cancers. The treatment plan during pregnancy is determined by:

- Tumor size
- If nearby lymph nodes have cancer
- How far along the pregnancy is
- The specific type of cervical cancer

If the cancer is at a very early stage, such as stage IA, most doctors believe it is safe to continue the pregnancy to term and have treatment several weeks after birth. Surgery options after birth for early-stage cancers include a hysterectomy, radical trachelectomy, or a cone biopsy.

If the cancer is stage IB or higher, then you and your doctor must decide whether to continue the pregnancy. If not, treatment would be radical hysterectomy and/or radiation. Sometimes chemotherapy can be given during the pregnancy (in the second or third trimester) to shrink the tumor.

If you decide to continue the pregnancy, the baby should be delivered by cesarean section (C-section) as soon as it is able to survive outside the womb. More advanced cancers typically need be treated immediately.

Hyperlinks

- 1. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html</u>
- 2. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html</u>

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