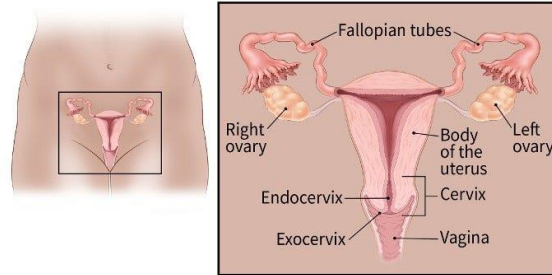


What is Cervical Cancer?

Cervix is the bottom part of uterus that connects to vagina. The **ectocervix** is the outer part that extends into vagina. **Endocervix** is canal between vagina and uterus body. Most cervical cancers are pre-cancers and start in the ectocervix of transformation zone. Cervical dysplasia or **cervical intraepithelial neoplasia (CIN)**, abnormal microscopic cells on the surface of cervix.



Types of Cervical Cancer:

- **Squamous Cell carcinoma:** most common 9/10 SCC. Cells in the exocervix. SCC most often begins in the transformation zone (where the exocervix joins the endocervix).
- **Adenocarcinoma:** develops from the mucus-producing gland cells of the endocervix, develop from glandular cells.
- **Neuroendocrine Carcinoma of the cervix (NECC)**

Symptoms:

- Abnormal vaginal bleeding, bleeding after vaginal sex, bleeding after menopause, bleeding, and spotting between periods, or having (menstrual) periods that are longer or heavier than usual. Bleeding after douching may also occur.
- Unusual vaginal discharge – might contain some blood, might occur between periods or after menopause.
- Pain during sex
- Pain in the pelvic region

Signs and symptoms seen with more advanced disease can include:

- Swelling of the legs
- Problems urinating or having a bowel movement.
- Blood in the urine

Risk Factors:

Modifiable

- Possibly linked to HPV (most common risk factor),
- Becoming sexually active at a young age (especially younger than 18 years old)
- Having many sexual partners
- Having one partner who is considered high risk (someone with HPV infection or who has many sexual partners)
- Human immunodeficiency virus (HIV), the virus that causes AIDS, weakens the immune system and puts people at higher risk for HPV infections.
- Chlamydia infections

- Long-term use of oral contraceptives
- Having multiple full-term pregnancies (3 or more)
- Age younger than 20 for first full term baby.
- Low-income women. They don't get screened or treated for cervical pre-cancers.
- Women with diet low in fruits and vegetables.

Nonmodifiable:

- Diethylstilbestrol (DES) exposure- Hormonal drug given between 1938-1971 to prevent miscarriages. Developed clear cell adenocarcinoma.
- Family history of cervical cancer. If mother and sister had cervical cancer, you have higher risk of developing.

Factors that might lower your risk:

Research suggests that women who had ever used an intrauterine device (IUD) had a lower risk of cervical cancer.

VACCINES:

- Gardasil, protects against 9 different HPV strains.

Screening:

- Should begin at age 25.
- Ages 25 to 65 – HPV test* every 5 years (If HPV testing is not available, screening may be done with either a co-test that combines an HPV test with a Papanicolaou (Pap) test every 5 years, or a Pap test alone every 3 years).
- Age 65 – those with regular and normal results on screening over previous 10 years and no history of CIN2, or more serious diagnosis within the past 25 years) can stop cervical cancer screening. Once stopped, it should not be started again.
- After a total hysterectomy – should stop screening unless the hysterectomy was done as a treatment for cervical cancer or serious pre-cancer.
- People who have had a hysterectomy without removal of the cervix (called a supra-cervical hysterectomy) should continue cervical cancer screening according to the guidelines above.

Testing for Cervical Cancers

- Medical history or physical exam (pelvic exam, pap test, or palpable lymph nodes)
- **Colposcopy** – weak solution of acetic acid is placed on cervix to make any abnormal areas easier to see. Colposcope inserted into vagina, small piece of tissue removed for colposcopic biopsy.
- **Endocervical curettage (endocervical scraping)** – Either a **curette** or a **brush** is inserted into the endocervical canal, to scrape the inside of the canal, and remove some of the tissues, to be sent to the lab to be checked.
- **Cone biopsy** – doctor removes a cone-shaped piece of tissue from the cervix (formed by the exocervix and the point or apex of the cone is from the endocervical canal). The tissue removed in the cone includes the transformation zone.

Imaging studies

These tests can determine if and where the cancer has spread. Aids in treatment plan.

Chest x-ray

Your chest may be x-rayed to see if cancer has spread to your lungs.

Computed tomography (CT)

Usually done if the tumor is larger or if there is concern about cancer spread.

Magnetic resonance imaging (MRI)

Look at the soft tissue parts of the body.

Positron emission tomography (PET scan)

A slightly radioactive form of sugar (known as FDG) is injected into the blood and collects mainly in cancer cells. This lets the doctor compare areas of higher radioactivity on the PET scan with a more detailed picture on the CT scan to determine if the cancer has spread to lymph nodes.

Intravenous urography

Intravenous urography (also known as **intravenous pyelogram**, or **IVP**) is an x-ray of the urinary system taken after a special dye is injected into a vein to search for abnormal areas in the urinary tract, caused by the spread of cervical cancer. The most common finding is that the cancer has blocked the ureters (tubes that connect the kidneys to the bladder). IVP is rarely used for patients with cervical cancer because CT and MRI are also good at finding abnormal areas in the urinary tract, as well as others not seen with an IVP.

Treatment:

Surgery

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 pre-cancers 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 loop electrosurgical excision procedure, LEEP or LEETZ procedure).

Surgery for invasive cervical cancer

Procedures to treat invasive cervical cancer are:

- **Hysterectomy**
 - **Simple** – 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.
 - **Radical hysterectomy**– 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.)
- **Trachelectomy** – removes the cervix and the upper part of the vagina but not the body of the uterus

Surgery to remove nearby lymph nodes.

Para-aortic lymph node sampling

During surgery for a radical hysterectomy, the lymph nodes next to the aorta are removed, this is called **para-aortic lymph node sampling**. **Nodes** are sent to the lab during the operation, and if negative, pelvic lymph nodes are removed. If positive, surgery may be stopped, and radiation and chemotherapy are given instead.

Pelvic lymph node dissection

Cancer can spread to lymph nodes in the pelvis. The surgeon removes some of these lymph nodes. This procedure is known as a **pelvic lymph node dissection** or **lymph node sampling**. Lymph nodes removal can lead to lymphedema.

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 [lymphedema](#).

Radiation

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

[External beam radiation therapy](#) (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.

Brachytherapy (internal radiation therapy)

[Brachytherapy](#), 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 [side effects](#) as 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 [Sex and the Women With Cancer](#).

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 [Sex and the Women With Cancer](#).

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 called [lymphedema](#).

Chemotherapy

the preferred treatment is [radiation](#) 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.

Targeted Drug Therapy

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.

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).

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.

- 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.

Regardless of whether there are PD-L1 proteins detected on the cancer cells, pembrolizumab can be used:

- Along with [concurrent chemoradiation](#) for advanced stage cervical cancer.

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.

Cervical Cancer Stages

After someone is diagnosed with cervical cancer, doctors will try to figure out if it has spread, and if so, how far. This process is called **staging**. The stage of a cancer describes the extent of the cancer in the body. It helps determine how serious the cancer is and [how best to treat it](#). **The stage is one of the most important factors in deciding how to treat the cancer and determining how successful treatment might be.**

To determine the cancer's stage after a cervical cancer diagnosis, doctors try to answer these questions:

- How far has the cancer grown into the cervix?
- Has the cancer reached nearby structures?
- Has the cancer spread to the nearby lymph nodes or to distant organs?

Information from [exams and tests](#) is used to determine the size of the tumor, how deeply the tumor has invaded tissues in and around the cervix, and its spread to distant places (metastasis). For more information see [Cancer Staging](#).

The **FIGO (International Federation of Gynecology and Obstetrics) staging system** is used most often for cancers of the female reproductive organs, including cervical cancer. For cervical cancer, the **clinical stage** is used and is based on the results of the doctor's physical exam, biopsies, imaging tests, and a few other tests that are done in some cases, such as cystoscopy and proctoscopy. It is not based on what is found during surgery. If surgery is done, a **pathologic stage** can be determined from the findings at surgery, but it does not change your clinical stage. Your treatment plan is based on the clinical stage. Cervical cancer stage ranges from stages I (1) through IV (4).

As a rule, the lower the number, the less the cancer has spread. A higher number, such as stage IV, means a more advanced cancer. And within a stage, an earlier letter means a lower stage. Cancers with similar stages tend to have a similar outlook and are often treated in much the same way.

Cervical cancer staging can be complex. If you have any questions about your stage, please ask your doctor to explain it to you in a way you understand. (An explanation of the FIGO system is in the stage table below.)

FIGO Stage		Stage description
I		<p>The cancer cells have grown from the surface of the cervix into deeper tissues of the cervix.</p> <p>Cancer has not spread to nearby lymph nodes.</p> <p>Cancer has not spread to distant sites.</p>
	IA	<p>There is a very small amount of cancer, and it can be seen only under a microscope.</p> <p>It has not spread to nearby lymph nodes.</p> <p>It has not spread to distant sites.</p>
	IA1	<p>The area of cancer can only be seen with a microscope and is less than 3 mm (about 1/8-inch) deep.</p> <p>It has not spread to nearby lymph nodes.</p> <p>It has not spread to distant sites.</p>
	IA2	<p>The area of cancer can only be seen with a microscope and is between 3 mm and 5 mm (about 1/5-inch) deep.</p> <p>It not has not spread to nearby lymph nodes.</p> <p>It has not spread to distant sites.</p>
	IB	<p>This includes stage I cancer that has spread deeper than 5 mm (about 1/5 inch) but is still limited to the cervix.</p> <p>It has not spread to nearby lymph nodes.</p> <p>It has not spread to distant sites.</p>
	IB1	<p>The cancer is deeper than 5 mm (about 1/5-inch) but not more than 2 cm (about 4/5-inch) in size.</p> <p>It has not spread to nearby lymph nodes.</p> <p>It has not spread to distant sites.</p>
	IB2	<p>The cancer is at least 2 cm in size but not larger than 4 cm.</p> <p>It has not spread to nearby lymph nodes.</p> <p>It has not spread to distant sites.</p>
	IB3	<p>The cancer is at least 4 cm in size and limited to the cervix.</p> <p>It has not spread to nearby lymph nodes.</p> <p>It has not spread to distant sites.</p>
		<p>The cancer has grown beyond the cervix and uterus, but hasn't spread to the walls of the pelvis or the lower part of the vagina.</p> <p>It has not spread to nearby lymph nodes.</p> <p>It has not spread to distant sites.</p>
II	IIA	<p>The cancer has grown beyond the cervix and uterus but has not spread into the tissues next to the cervix (called the parametria).</p>

III		<p>It has not spread to nearby lymph nodes.</p> <p>It has not spread to distant sites.</p>
	IIA1	<p>The cancer is not larger than 4 cm (about 1 3/5 inches).</p> <p>It not has not spread to nearby lymph nodes.</p> <p>It has not spread to distant sites.</p>
	IIA2	<p>The cancer is 4 cm or larger.</p> <p>It has not spread to nearby lymph nodes.</p> <p>It has not spread to distant sites.</p>
	IIB	<p>The cancer has grown beyond the cervix and uterus and has spread into the tissues next to the cervix (the parametria).</p> <p>It has not spread to nearby lymph nodes.</p> <p>It has not spread to distant sites.</p>
		<p>The cancer has spread to the lower part of the vagina or the walls of the pelvis. The cancer may be blocking the ureters (tubes that carry urine from the kidneys to the bladder).</p> <p>It might or might not have not spread to nearby lymph nodes.</p> <p>It has not spread to distant sites.</p>
	IIIA	<p>The cancer has spread to the lower part of the vagina but not the walls of the pelvis.</p> <p>It has not spread to nearby lymph nodes.</p> <p>It has not spread to distant sites.</p>
IV	IIIB	<p>The cancer has grown into the walls of the pelvis and/or is blocking one or both ureters causing kidney problems (called hydronephrosis).</p> <p>It has not spread to nearby lymph nodes.</p> <p>It has not spread to distant sites.</p>
	IIIC	<p>The cancer can be any size.</p> <p>Imaging tests or a biopsy show the cancer has spread to nearby pelvic lymph nodes (IIIC1) or para-aortic lymph nodes (IIIC2).</p> <p>It has not spread to distant sites.</p>
		<p>The cancer has grown into the bladder or rectum or to far away organs like the lungs or bones.</p>
	IVA	<p>The cancer has spread to the bladder or rectum or it is growing out of the pelvis.</p>
	IVB	<p>The cancer has spread to distant organs outside the pelvic area, such as distant lymph nodes, lungs or bones.</p>

Surgery for Cervical Cancer

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 pre-cancers 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 loop electrosurgical excision procedure, 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](#).

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.

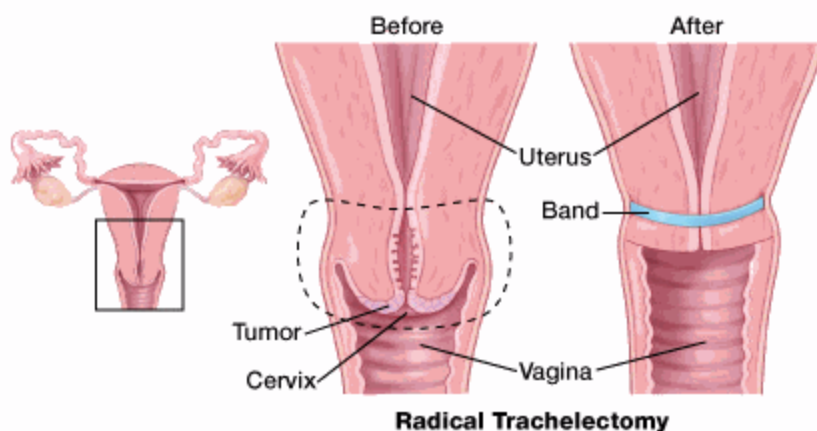
Possible side effects: Because the uterus is removed, this surgery results in infertility. Because some of the nerves to the bladder are removed, some women have problems emptying their bladder after this operation and may need a catheter for a time. Complications are unusual but could include bleeding, 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 [lymphedema](#) (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 Cancer](#).

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 Guide](#).

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 [Colostomy Guide](#)). 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 Cancer](#).

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 [Lymphedema](#).

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 [lymphedema](#). 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.

Radiation Therapy for Cervical Cancer

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

[External beam radiation therapy](#) (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 effects](#) 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)

[Brachytherapy](#), 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 [side effects](#) as 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 [Sex and the Women With Cancer](#).

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 [Sex and the Women With Cancer](#).

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 called [lymphedema](#). If you are having side effects from radiation treatment, discuss them with your cancer care team.

Chemotherapy for Cervical Cancer

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 [radiation](#) 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 [central venous catheters](#) (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 [side effects](#). 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 low](#). 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 pre-menopausal 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 [damage nerves](#) 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 [peripheral neuropathy](#). 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 [Chemotherapy](#).

To learn about some of the side effects listed here and how to manage them, see [Managing Cancer-related Side Effects](#).

Targeted Drug Therapy for Cervical Cancer

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.

Immunotherapy for Cervical Cancer

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.
- 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.

Regardless of whether there are PD-L1 proteins detected on the cancer cells, pembrolizumab can be used:

- Along with [concurrent chemoradiation](#) for advanced stage cervical cancer.

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.

REFERENCES are available via American Cancer Society website

[Cervical Cancer Statistics | Types of Cervical Cancer | American Cancer Society](#)

[Cervical Cancer Causes & Risk Factors | Cervical Cancer Prevention | American Cancer Society](#)

[Cervical Cancer Detection & Diagnosis | Cervical Cancer Staging | American Cancer Society](#)

[Cervical Cancer Treatment | How Is Cervical Cancer Treated? | American Cancer Society](#)

Eifel P, Klopp AH, Berek JS, and Konstantinopoulos A. Chapter 74: Cancer of the Cervix, Vagina, and Vulva. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 11th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2019.

Jhungrán A, Russell AH, Seiden MV, Duska LR, Goodman A, Lee S, et al. Chapter 84: Cancers of the Cervix, Vulva, and Vagina. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 6th ed. Philadelphia, Pa: Elsevier; 2020.

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology: Cervical Cancer. Version 5.2019. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf on December 12, 2019.

Eifel P, Klopp AH, Berek JS, and Konstantinopoulos A. Chapter 74: Cancer of the Cervix, Vagina, and Vulva. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 11th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2019.

Fontham, ETH, Wolf, AMD, Church, TR, et al. Cervical Cancer Screening for Individuals at Average Risk: 2020 Guideline Update from the American Cancer Society. *CA Cancer J Clin*. 2020.
<https://doi.org/10.3322/caac.21628>.

Jhungrán A, Russell AH, Seiden MV, Duska LR, Goodman A, Lee S, et al. Chapter 84: Cancers of the Cervix, Vulva, and Vagina. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 6th ed. Philadelphia, Pa: Elsevier; 2020.

Khieu M, Butler SL. High Grade Squamous Intraepithelial Lesion. StatPearls. PMID: 28613479. 2022.

National Cancer Institute. Physician Data Query (PDQ). Cervical Cancer Treatment – Health Professional Version. 2019. <https://www.cancer.gov/types/cervical/hp/cervical-treatment-pdq>. Updated February 6, 2019. Accessed on October 30, 2019.