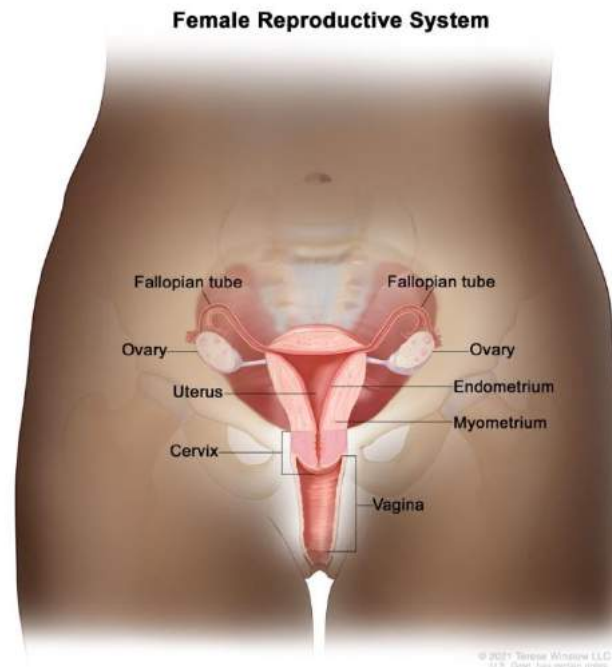


The cervix is the lower part of the womb (uterus). The uterus has two parts — the upper part (body) where a baby grows, and the lower part (cervix). The cervix connects the body of the uterus to the vagina (birth canal).



Cervical cancer, or cancer of the cervix, begins on the surface of the cervix. As per Globocan 2020 cervical cancer is the fourth most common cancer among females worldwide and second most common cancer among females in India. There are two main types of cancer of the cervix — squamous cell carcinomas and adenocarcinomas. About 80% to 90% are squamous cell carcinomas, 10%-20% are adenocarcinomas and other varieties are rare.

Various strains of the human papillomavirus (HPV), a sexually transmitted infection, play a role in causing most cervical cancer. When exposed to HPV, a woman's immune system typically prevents the virus from doing harm. In a small group of women, however, the virus survives for years, contributing to the process that causes some cells on the surface of the cervix to become cancer cells.

SYMPTOMS

Early-stage cervical cancer generally produces no signs or symptoms.

Signs and symptoms of more-advanced cervical cancer include:

- Vaginal bleeding after intercourse, between periods or after menopause
- Watery, bloody vaginal discharge that may be heavy and have a foul odor
- Pelvic pain or pain during intercourse

RISK FACTORS

Human papillomavirus (HPV) infection is the major risk factor for cervical cancer.

Anything that increases your chance of getting a disease is called a risk factor. Having a risk factor does not mean that you will get cancer; not having risk factors doesn't mean that you will not get cancer. Talk to your doctor if you think you may be at risk for cervical cancer.

Risk factors for cervical cancer include the following:

- Being infected with human papillomavirus (HPV). This is the most important risk factor for cervical cancer.
- Being exposed to the drug DES (diethylstilbestrol) while in the mother's womb.

In women who are infected with HPV, the following risk factors add to the increased risk of cervical cancer:

- Giving birth to many children.
- Smoking cigarettes.
- Using oral contraceptives ("the Pill") for a long time.

There are also risk factors that increase the risk of HPV infection:

- Having a weakened immune system caused by immunosuppression. Immunosuppression weakens the body's ability to fight infections and other diseases. The body's ability to fight HPV infection may be lowered by long-term immunosuppression from:
 - being infected with human immunodeficiency virus (HIV).
- Being sexually active at a young age.
- Having many sexual partners.

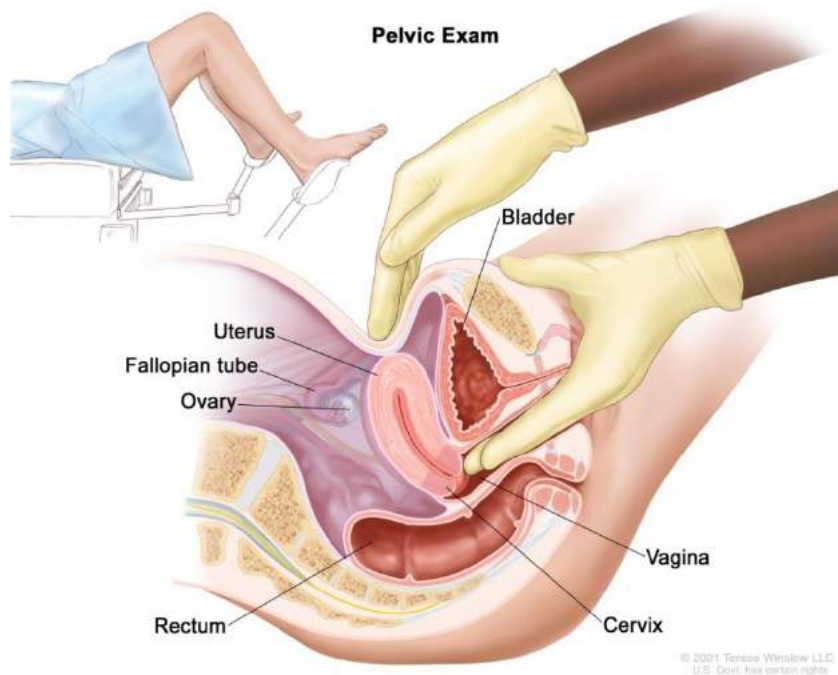
Older age is a main risk factor for most cancers. The chance of getting cancer increases as you get older.

HOW IS CERVICAL CANCER DIAGNOSED?

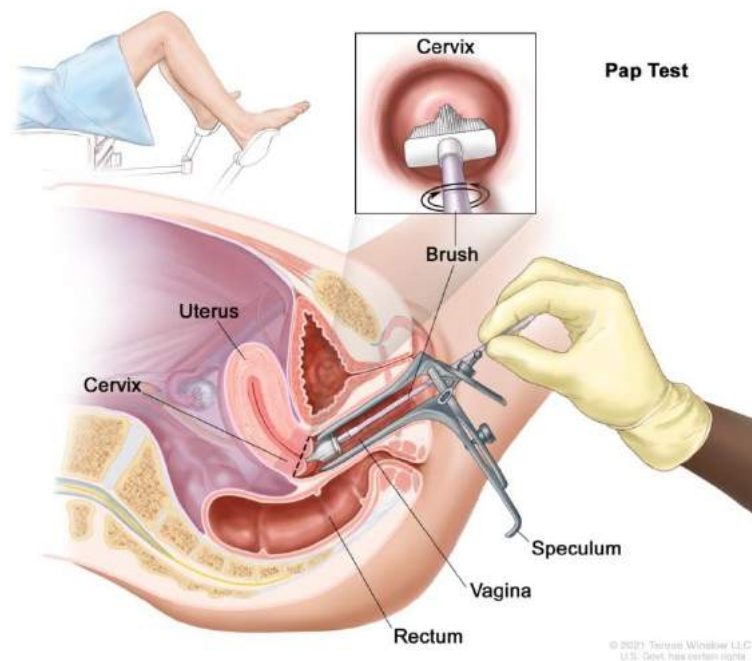
Tests that examine the cervix are used to diagnose cervical cancer.

The following procedures may be used:

- **Physical exam and health history:** An exam of the body to check general signs of health, including checking for signs of disease, such as lumps or anything else that seems unusual. A history of the patient's health habits and past illnesses and treatments will also be taken.
- **Pelvic exam:** An exam of the vagina, cervix, uterus, fallopian tubes, ovaries, and rectum. A speculum is inserted into the vagina and the doctor or nurse looks at the vagina and cervix for signs of disease. A Pap test of the cervix is usually done. The doctor or nurse also inserts one or two lubricated, gloved fingers of one hand into the vagina and places the other hand over the lower abdomen to feel the size, shape, and position of the uterus and ovaries. The doctor or nurse also inserts a lubricated, gloved finger into the rectum to feel for lumps or abnormal areas



Pap test: A procedure that uses a small brush to collect cells from the surface of the cervix and the area around it. The cells are viewed under a microscope to find out if they are abnormal. This procedure is also called a Pap smear.



Together, pelvic exams and Pap smears can detect most cases of cervical cancer. For an accurate diagnosis, your doctor will visually examine the cervix and take a tissue sample of any apparent abnormality for biopsy.

Human papillomavirus (HPV) test: A laboratory test used to check DNA or RNA for certain types of HPV infection. Cells are collected from the cervix and DNA or RNA from the cells is checked to find out if an infection is caused by a type of HPV that is linked to cervical cancer. This test may be done using the sample of cells removed during a Pap test. This test may also be done if the results of a Pap test show certain abnormal cervical cells.

Colposcopy: A procedure in which a colposcope (a lighted, magnifying instrument) is used to check the vagina and cervix for abnormal areas. Tissue samples may be taken using a curette (spoon-shaped instrument) or a brush and checked under a microscope for signs of disease.

Biopsy: If abnormal cells are found in a Pap test, the doctor may do a biopsy. A sample of tissue is cut from the cervix and viewed under a microscope by a pathologist to check for signs of cancer. A biopsy that removes only a small amount of tissue is usually done in the doctor's office. A woman may need to go to a hospital for a cervical cone biopsy (removal of a larger, cone-shaped sample of cervical tissue)

If the biopsy confirms cancer, further tests will determine whether the disease has spread (metastasized). These tests might include liver and kidney function studies; blood and urine tests; and X-rays of the bladder, rectum, bowels, and abdominal cavity. This process is called staging.

The following tests and procedures may be used in the staging process:

- **CT scan (CAT scan):** A procedure that makes a series of detailed pictures of areas inside the body, taken from different angles. The pictures are made by a computer linked to an x-ray machine. A dye may be injected into a vein or swallowed to help the organs or tissues show up more clearly. This procedure is also called computed tomography, computerized tomography, or computerized axial tomography.
- **PET scan (positron emission tomography scan):** A procedure to find malignant tumor cells in the body. A small amount of radioactive glucose (sugar) is injected into a vein. The PET scanner rotates around the body and makes a picture of where glucose is being used in the body. Malignant tumor cells show up brighter in the picture because they are more active and take up more glucose than normal cells do.
- **MRI (magnetic resonance imaging):** A procedure that uses a magnet, radio waves, and a computer to make a series of detailed pictures of areas inside the body. This procedure is also called nuclear magnetic resonance imaging (NMRI).
- **Ultrasound exam:** A procedure in which high-energy sound waves (ultrasound) are bounced off internal tissues or organs and make echoes. The echoes form a picture of body tissues called a sonogram. This picture can be printed to be looked at later.
- **Chest x-ray:** An x-ray of the organs and bones inside the chest. An x-ray is a type of energy beam that can go through the body and onto film, making a picture of areas inside the body.
- **Cystoscopy:** A procedure to look inside the bladder and urethra to check for abnormal areas. A cystoscope is inserted through the urethra into the bladder. A cystoscope is a thin, tube-like instrument with a light and a lens for viewing. It may also have a tool to remove tissue samples, which are checked under a microscope for signs of cancer.

The results of these tests are viewed together with the results of the original tumor biopsy to determine the cervical cancer stage.

There are three ways that cancer spreads in the body.

Cancer can spread through tissue, the lymph system, and the blood:

- Tissue. The cancer spreads from where it began by growing into nearby areas.
- Lymph system. The cancer spreads from where it began by getting into the lymph system. The cancer travels through the lymph vessels to other parts of the body.
- Blood. The cancer spreads from where it began by getting into the blood. The cancer travels through the blood vessels to other parts of the body.

Cancer may spread from where it began to other parts of the body.

When cancer spreads to another part of the body, it is called metastasis. Cancer cells break away from where they began (the primary tumor) and travel through the lymph system or blood.

The metastatic tumor is the same type of cancer as the primary tumor. For example, if cervical cancer spreads to the lung, the cancer cells in the lung are actually cervical cancer cells. The disease is metastatic cervical cancer, not lung cancer

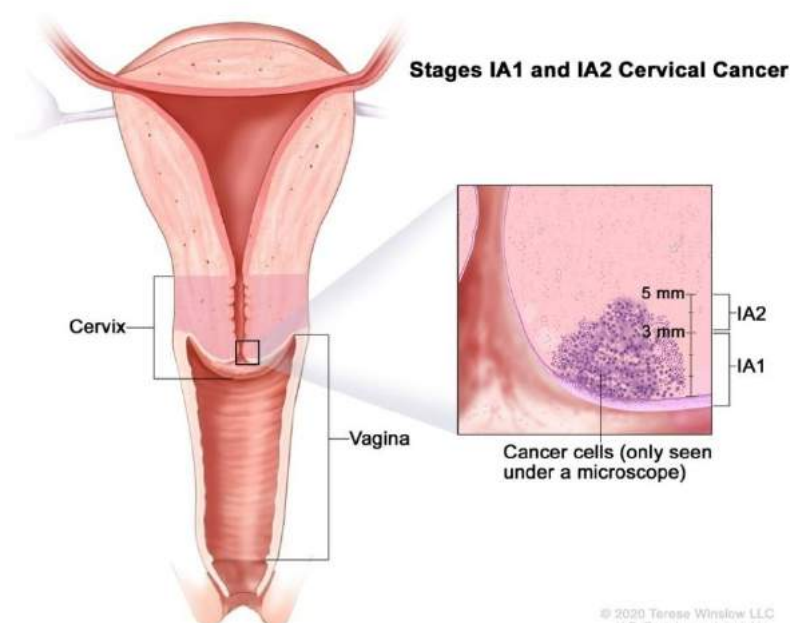
THE STAGES OF CERVICAL CANCER

Stage I

In stage I, cancer has formed and is found in the cervix only.

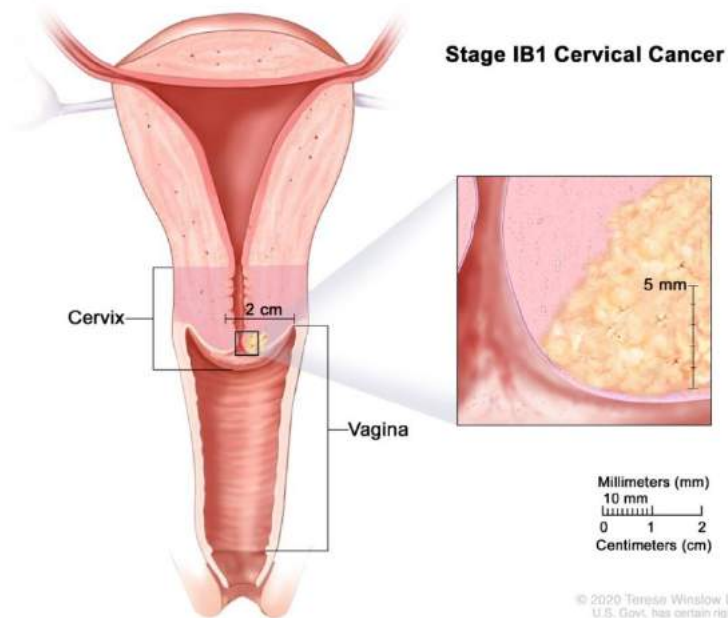
Stage I is divided into stages IA and IB, based on the size of the tumor and the deepest point of tumor invasion.

- Stage IA: Stage IA is divided into stages IA1 and IA2, based on the deepest point of tumor invasion.



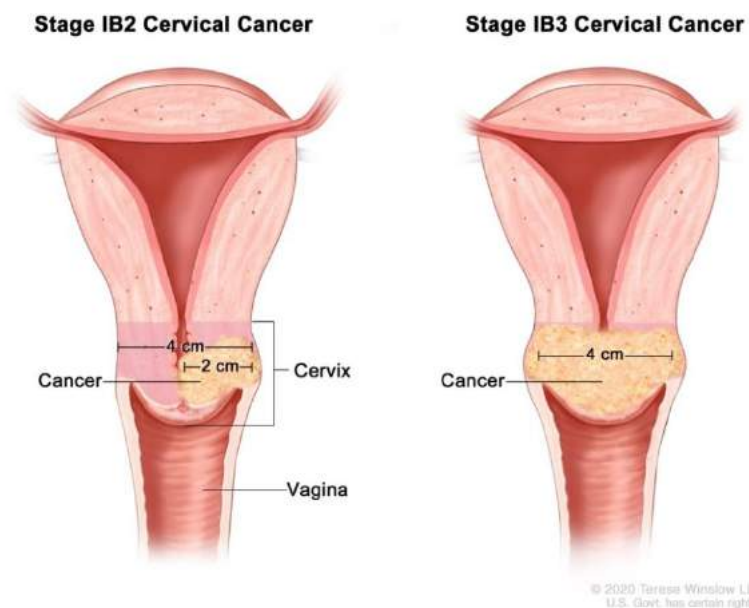
Stage IB: Stage IB is divided into stages IB1, IB2, and IB3, based on the size of the tumor and the deepest point of tumor invasion.

- In stage IB1, the tumor is 2 centimeters or smaller and the deepest point of tumor invasion is more than 5 millimeters.



In stage IB2, the tumor is larger than 2 centimeters but not larger than 4 centimeters.

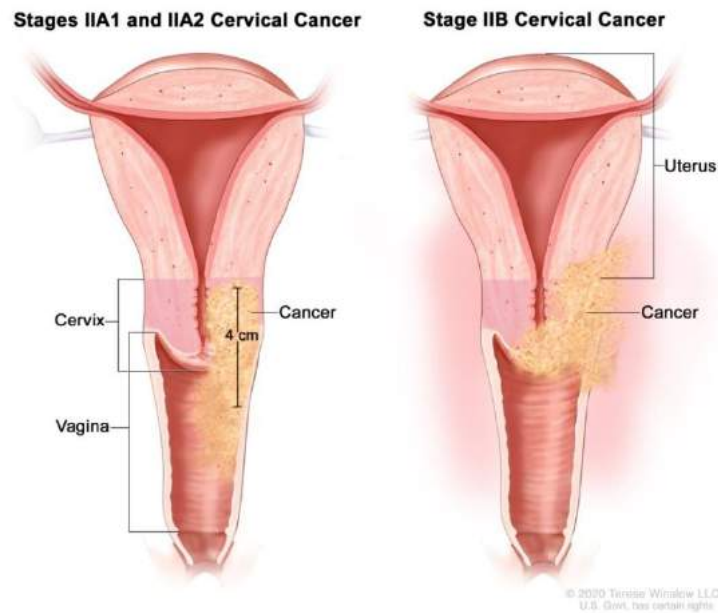
In stage IB3, the tumor is larger than 4 centimeters.



Stage II

In stage II, cancer has spread to the upper two-thirds of the vagina or to the tissue around the uterus.

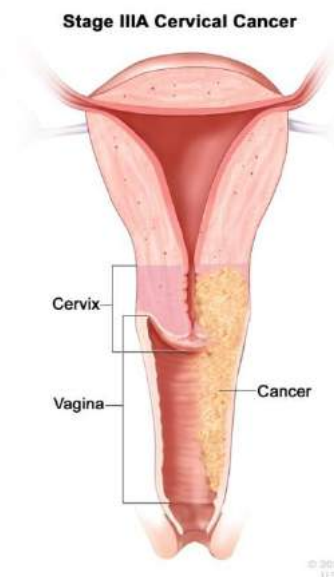
Stage II is divided into stages IIA and IIB, based on how far the cancer has spread.



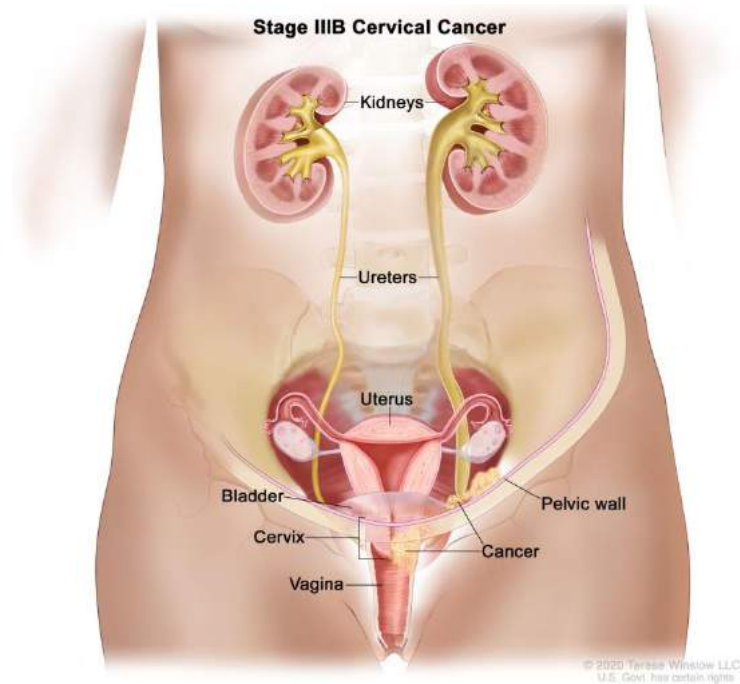
Stage III

In stage III, cancer has spread to the lower third of the vagina and/or to the pelvic wall, and/or has caused kidney problems, and/or involves lymph nodes. Stage III is divided into IIIA, IIIB, and IIIC

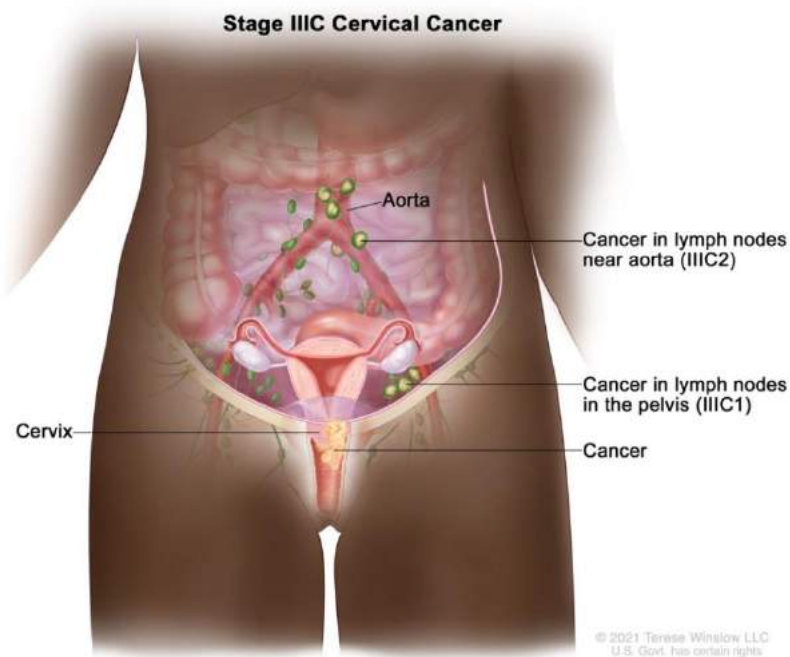
- Stage IIIA: Cancer has spread to the lower third of the vagina but has not spread to the pelvic wall.



Stage IIIB: Cancer has spread to the pelvic wall; and/or the tumor has become large enough to block one or both ureters or has caused one or both kidneys to get bigger or stop working.



Stage IIIC: Stage IIIC is divided into stages IIIC1 and IIIC2, based on the spread of cancer to the lymph nodes.

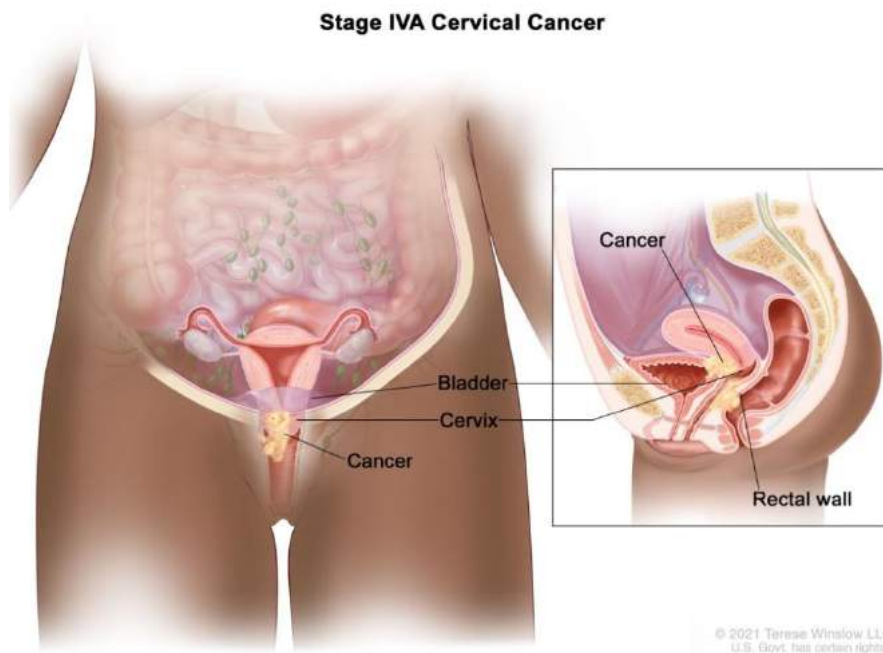


Stage IV

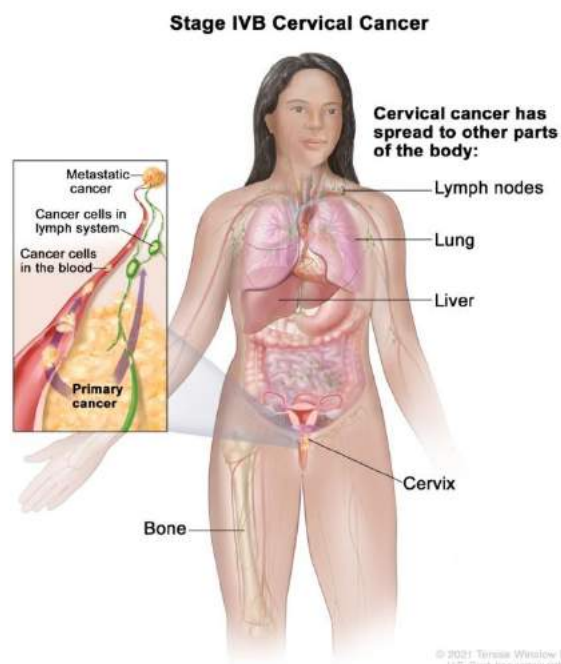
In stage IV, cancer has spread beyond the pelvis, or has spread to the lining of the bladder or rectum, or has spread to other parts of the body.

Stage IV is divided into stages IVA and IVB, based on where the cancer has spread.

- Stage IVA: Cancer has spread to nearby pelvic organs, such as the bladder or rectum.



Stage IVB: Cancer has spread to other parts of the body, such as the liver, lungs, bones, or distant lymph nodes.



TREATMENT OPTIONS

Treatment options depend on the following:

- The stage of the cancer.
- The type of cervical cancer.
- The patient's desire to have children.
- The patient's age.

There are different types of treatment for patients with cervical cancer.

- Surgery
- Radiation therapy
- Chemotherapy
- Targeted therapy
- Immunotherapy
- Follow-up tests are needed.

Surgery

Surgery (removing the cancer in an operation) is sometimes used to treat cervical cancer. The following surgical procedures may be used:

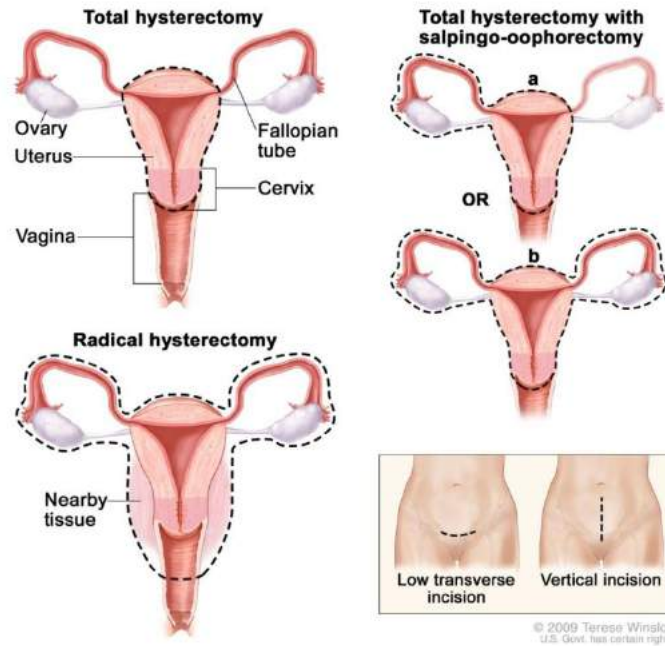
- Conization: A procedure to remove a cone-shaped piece of tissue from the cervix and cervical canal. A pathologist views the tissue under a microscope to look for cancer cells. Conization may be used to diagnose or treat a cervical condition. This procedure is also called a cone biopsy.

Conization may be done using one of the following procedures:

- Cold-knife conization: A surgical procedure that uses a scalpel (sharp knife) to remove abnormal tissue or cancer.
- Loop electrosurgical excision procedure (LEEP): A surgical procedure that uses electrical current passed through a thin wire loop as a knife to remove abnormal tissue or cancer.
- Laser surgery: A surgical procedure that uses a laser beam (a narrow beam of intense light) as a knife to make bloodless cuts in tissue or to remove a surface lesion such as a tumor.

The type of conization procedure used depends on where the cancer cells are in the cervix and the type of cervical cancer.

- Total hysterectomy: Surgery to remove the uterus, including the cervix. If the uterus and cervix are taken out through the vagina, the operation is called a vaginal hysterectomy. If the uterus and cervix are taken out through a large incision (cut) in the abdomen, the operation is called a total abdominal hysterectomy. If the uterus and cervix are taken out through a small incision in the abdomen using a laparoscope, the operation is called a total laparoscopic hysterectomy.



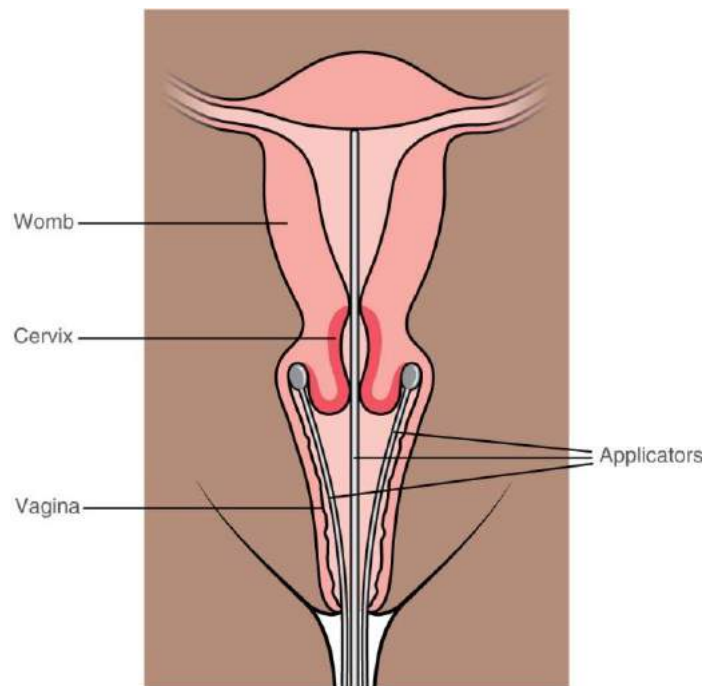
- **Radical hysterectomy**: Surgery to remove the uterus, cervix, part of the vagina, and a wide area of ligaments and tissues around these organs. The ovaries, fallopian tubes, or nearby lymph nodes may also be removed.
- **Modified radical hysterectomy**: Surgery to remove the uterus, cervix, upper part of the vagina, and ligaments and tissues that closely surround these organs. Nearby lymph nodes may also be removed. In this type of surgery, not as many tissues and/or organs are removed as in a radical hysterectomy.
- **Radical trachelectomy**: Surgery to remove the cervix, nearby tissue and lymph nodes, and the upper part of the vagina. The uterus and ovaries are not removed.
- **Bilateral salpingo-oophorectomy**: Surgery to remove both ovaries and both fallopian tubes. **Pelvic exenteration**: Surgery to remove the lower colon, rectum, and bladder. The cervix, vagina, ovaries, and nearby lymph nodes are also removed. Artificial openings (stoma) are made for urine and stool to flow from the body to a collection bag. Plastic surgery may be needed to make an artificial vagina after this operation.

Radiation therapy

Radiation therapy is a cancer treatment that uses high-energy x-rays or other types of radiation to kill cancer cells or keep them from growing. There are two types of radiation therapy:

- **External radiation therapy** uses a machine outside the body to send radiation toward the area of the body with cancer. Certain ways of giving radiation therapy can help keep radiation from damaging nearby healthy tissue. This type of radiation therapy includes the following:

- Intensity-modulated radiation therapy (IMRT): IMRT is a type of 3-dimensional (3-D) radiation therapy that uses a computer to make pictures of the size and shape of the tumor. Thin beams of radiation of different intensities (strengths) are aimed at the tumor from many angles.
 - Image Guided Radiotherapy (IGRT): it uses image guidance during radiotherapy
- Internal radiation therapy (Brachytherapy) uses a radioactive substance sealed in needles, seeds, wires, or catheters that are placed directly into or near the cancer.



The way the radiation therapy is given depends on the type and stage of the cancer being treated. External and internal radiation therapy are used to treat cervical cancer, and may also be used as palliative therapy to relieve symptoms and improve quality of life.

Chemotherapy

Chemotherapy is a cancer treatment that uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing. When chemotherapy is taken by mouth or injected into a vein or muscle, the drugs enter the bloodstream and can reach cancer cells throughout the body (systemic chemotherapy).

Targeted therapy

Targeted therapy is a type of treatment that uses drugs or other substances to identify and attack specific cancer cells. Targeted therapies usually cause less harm to normal cells than chemotherapy or radiation therapy do.

Monoclonal antibody therapy is a type of targeted therapy.

Bevacizumab is a monoclonal antibody that binds to a protein called vascular endothelial growth factor (VEGF) and may prevent the growth of new blood vessels that tumors need to grow. Bevacizumab is used to treat cervical cancer that has metastasized (spread to other parts of the body) and recurrent cervical cancer.

Immunotherapy

Immunotherapy is a treatment that uses the patient's immune system to fight cancer. Substances made by the body or made in a laboratory are used to boost, direct, or restore the body's natural defenses against cancer. This cancer treatment is a type of biologic therapy.

Immune checkpoint inhibitor therapy is a type of immunotherapy.

- PD-1 and PD-L1 inhibitor therapy: PD-1 is a protein on the surface of T cells that helps keep the body's immune responses in check. PD-L1 is a protein found on some types of cancer cells. When PD-1 attaches to PD-L1, it stops the T cell from killing the cancer cell. PD-1 and PD-L1 inhibitors keep PD-1 and PD-L1 proteins from attaching to each other. This allows the T cells to kill cancer cells. Pembrolizumab is a type of PD-1 inhibitor.

Follow-up tests are needed.

Some of the tests that were done to diagnose the cancer or to find out the stage of the cancer may be repeated. Some tests will be repeated in order to see how well the treatment is working. Decisions about whether to continue, change, or stop treatment may be based on the results of these tests.

Some of the tests will continue to be done from time to time after treatment has ended. The results of these tests can show if your condition has changed or if the cancer has recurred (come back). These tests are sometimes called follow-up tests or check-ups.

Your doctor will ask if you have any of the following signs or symptoms, which may mean the cancer has come back:

- Pain in the abdomen, back, or leg.
- Swelling in the leg.
- Trouble urinating.
- Cough.
- Feeling tired.

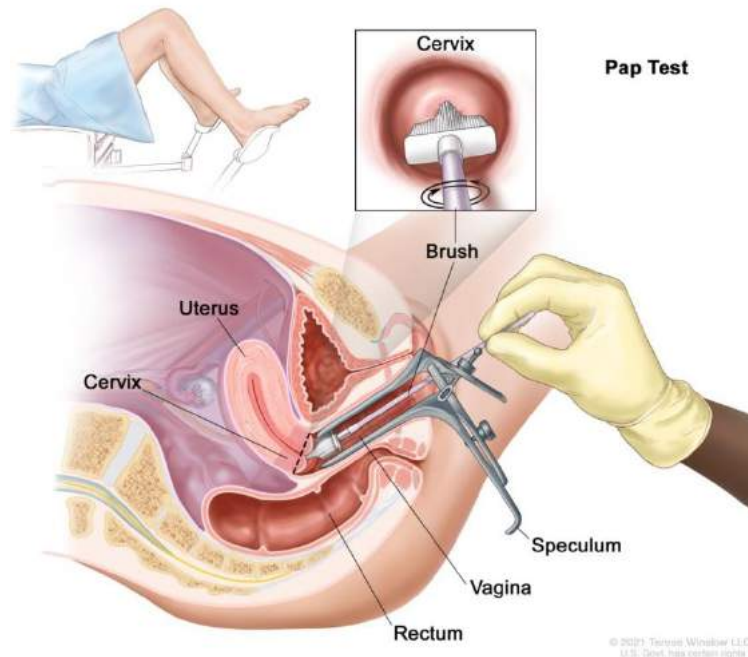
For cervical cancer, follow-up tests are usually done every 3 to 4 months for the first 2 years, followed by check-ups every 6 months. The check-up includes a current health history and exam of the body to check for signs and symptoms of recurrent cervical cancer and for late effects of treatment.

SCREENING AND PREVENTION

What is screening?

Screening is looking for cancer before a person has any symptoms. This can help find cancer at an early stage. When abnormal tissue or cancer is found early, it may be easier to treat. By the time symptoms appear, cancer may have begun to spread

Pap test: A procedure that uses a small brush to collect cells from the surface of the cervix and the area around it. The cells are viewed under a microscope to find out if they are abnormal. This procedure is also called a Pap smear.



Together, pelvic exams and Pap smears can detect most cases of cervical cancer. For an accurate diagnosis, your doctor will visually examine the cervix and take a tissue sample of any apparent abnormality for biopsy.

Human papillomavirus (HPV) test: A laboratory test used to check DNA or RNA for certain types of HPV infection. Cells are collected from the cervix and DNA or RNA from the cells is checked to find out if an infection is caused by a type of HPV that is linked to cervical cancer. This test may be done using the sample of cells removed during a Pap test. This test may also be done if the results of a Pap test show certain abnormal cervical cells.

Starting from the age of 21 years Pap test can be repeated every 3 years. Pap test combined with HPV testing can be repeated every 5 years

The Pap test is not a helpful screening test for cervical cancer in the following groups of women:

- Women who are younger than 21 years.

- Women who have had a total hysterectomy (surgery to remove the uterus and cervix) for a condition that is not cancer.
- Women who are aged 65 years or older and have a Pap test result that shows no abnormal cells. These women are very unlikely to have abnormal Pap test results in the future.

What is prevention?

Cancer prevention is action taken to lower the chance of getting cancer. By preventing cancer, the number of new cases of cancer in a group or population is lowered. Hopefully, this will lower the number of deaths caused by cancer.

Avoiding risk factors and increasing protective factors may help prevent cancer.

The following are *risk* factors for cervical cancer:

- HPV infection
- DES

In women who are infected with HPV, other risk factors add to the increased risk of cervical cancer:

- Giving birth to many children
- Using oral contraceptives for a long time
- Smoking cigarettes

The following increase the risk of HPV infection:

- Having a weakened immune system
- Being sexually active at a young age or having many sexual partners

The following *protective* factors decrease the risk of cervical cancer:

- Getting an HPV vaccine
- Using barrier protection during sexual activity