

HPV and Cervical Cancer

Original links: http://www.cdc.gov/hpv/cancer.html http://www.cdc.gov/cancer/cervical/index.htm

Key Points

- Some types of sexually transmitted human papillomaviruses (HPVs) can cause genital warts. Other types, called high-risk or oncogenic HPVs, can cause cancer.
- High-risk HPVs cause virtually all cervical cancers. They also cause most anal cancers and some vaginal, vulvar, penile, and oropharyngeal cancers.
- Most infections with high-risk HPVs do not cause cancer. Many HPV infections go away on their own within 1 to 2 years. However, infections that last for many years increase a person's risk of developing cancer.

1. What are HPVs?

HPVs, also called <u>human papillomaviruses</u>, are a group of more than 150 related <u>viruses</u>. More than 40 of these viruses can be easily spread through direct skin-toskin contact during vaginal, and, and oral sex (<u>1</u>).

HPV <u>infections</u> are the most common sexually transmitted infections in the United States. In fact, more than half of sexually active people are infected with one or more HPV types at some point in their lives. Recent research indicates that, at any point in time, 42.5 percent of women have genital HPV infections, whereas less than 7 percent of adults have oral HPV infections (2, 3).

Sexually transmitted HPVs fall into two categories:

- Low-risk HPVs, which do not cause cancer but can cause skin <u>warts</u> (technically known as condylomata acuminata) on or around the genitals or anus. For example, HPV types 6 and 11 cause 90 percent of all genital warts.
- High-risk or oncogenic HPVs, which can cause cancer. At least a dozen high-risk HPV types have been identified. Two of these, HPV types 16 and 18, are responsible for the majority of HPV-caused cancers.
- 2. What is the association between HPV infection and cancer?

High-risk HPV infection accounts for approximately 5 percent of all cancers worldwide (<u>4</u>). However, most high-risk HPV infections occur without any symptoms, go away within 1 to 2 years, and do not cause cancer. These transient infections may cause cytologic abnormalities, or abnormal cell changes, that go away on their own.

Some HPV infections, however, can persist for many years. Persistent infections with high-risk HPV types can lead to more serious cytologic abnormalities or lesions that, if untreated, may progress to cancer.

3. Which cancers are caused by HPVs?

Virtually all cervical cancers are caused by HPV infections, with just two HPV types, 16 and 18, responsible for about 70 percent of all cases (5, 6). HPV also causes anal cancer, with about 85 percent of all cases caused by HPV-16. HPV types 16 and 18 have also been found to cause close to half of vaginal, vulvar, and penile cancers (7).

Most recently, HPV infections have been found to cause cancer of the oropharynx, which is the middle part of the throat including the soft palate, the base of the tongue, and the tonsils. In the United States, more than half of the cancers diagnosed in the oropharynx are linked to HPV-16 ($\underline{8}$).

The incidence of HPV-associated oropharyngeal cancer has increased during the past 20 years, especially among men. It has been estimated that, by 2020, HPV will cause more oropharyngeal cancers than cervical cancers in the United States (9).

Other factors may increase the risk of developing cancer following a high-risk HPV infection (5). These other factors include the following:

- Smoking
- Having a weakened immune system
- Having many children (for increased risk of cervical cancer)
- Long-term oral contraceptive use (for increased risk of cervical cancer)
- Poor oral hygiene (for increased risk of oropharyngeal cancer)
- Chronic inflammation

4. Can HPV infection be prevented?

The most reliable way to prevent infection with either a high-risk or a low-risk HPV is to avoid any skin-to-skin oral, anal, or genital contact with another person (1). For those who are sexually active, a long-term, mutually monogamous relationship with an uninfected partner is the strategy most likely to prevent HPV infection (1). However, because of the lack of symptoms it is hard to know whether a partner who has been sexually active in the past is currently infected with HPV.

Research has shown that correct and consistent use of condoms can reduce the transmission of HPVs between sexual partners (10). Areas not covered by a condom can be infected with the virus, though (1), so condoms are unlikely to provide complete protection against virus spread.

The Food and Drug Administration (FDA) has approved two HPV vaccines: <u>Gardasil</u>® for the prevention of cervical, anal, vulvar, and vaginal cancer, as well as precancerous lesions in these tissues and genital warts caused by HPV infection; and <u>Cervarix</u>® for the prevention of cervical cancer and precancerous cervical lesions caused by HPV infection. Both vaccines are highly effective in preventing infections with HPV types 16 and 18. Gardasil also prevents infection with HPV types 6 and 11. These vaccines have not been approved for prevention of penile or oropharyngeal cancer.

More information about HPV vaccines is available in the NCI fact sheet <u>Human</u> <u>Papillomavirus (HPV) Vaccines</u>.

5. How are HPV infections detected?

HPV infections can be detected by testing a sample of cells to see if they contain viral DNA or RNA.

The most common test detects DNA from several high-risk HPV types, but it cannot identify the type(s) that are present. Another test is specific for DNA from HPV types 16 and 18, the two types that cause most HPV-associated cancers. A third test can detect DNA from several high-risk HPV types and can indicate whether HPV-16 or HPV-18 is present. A fourth test detects RNA from the most common high-risk HPV types. These tests can detect HPV infections before cell abnormalities are evident.

Theoretically, the <u>HPV DNA</u> and RNA tests could be used to identify HPV infections in cells taken from any part of the body. However, the tests are approved by the FDA for only two indications: for follow-up testing of women who seem to have abnormal <u>Pap test</u> results and for cervical cancer screening in combination with a Pap test among women over age 30.

There are no FDA-approved tests to detect HPV infections in men. There are also no currently recommended screening methods similar to a Pap test for detecting cell changes caused by HPV infection in anal, vulvar, vaginal, penile, or oropharyngeal tissues. However, this is an area of ongoing research.

6. What are treatment options for HPV-infected individuals?

There is currently no medical treatment for HPV infections. However, the genital warts and precancerous lesions resulting from HPV infections can be treated.

Methods commonly used to treat precancerous cervical lesions include <u>cryosurgery</u> (freezing that destroys tissue), <u>LEEP</u> (loop electrosurgical excision procedure, or the removal of cervical tissue using a hot wire loop), surgical <u>conization</u> (surgery with a scalpel, a laser, or both to remove a cone-shaped piece of tissue from the cervix and cervical canal), and laser vaporization conization (use of a laser to destroy cervical tissue).

Treatments for other types of precancerous lesions caused by HPV (vaginal, vulvar, penile, and anal lesions) and genital warts include topical chemicals or drugs, excisional surgery, cryosurgery, electrosurgery, and laser surgery. More information about the treatment of genital warts can be found in the Centers for Disease Control and Prevention (CDC) <u>Sexually Transmitted Diseases Treatment</u> <u>Guidelines, 2010</u>.

HPV-infected individuals who develop cancer generally receive the same treatment as patients whose tumors do not harbor HPV infections, according to the type and stage of their tumors. However, people who are diagnosed with HPV-positive oropharyngeal cancer may be treated differently than people with oropharyngeal cancers that are HPV-negative. Recent research has shown that patients with HPV-positive oropharyngeal tumors have a better prognosis and may do just as well on less intense treatment. An ongoing clinical trial is investigating this question.

7. How do high-risk HPVs cause cancer?

HPVs infect epithelial cells. These cells, which are organized in layers, cover the inside and outside surfaces of the body, including the skin, the throat, the genital tract, and the anus. Because HPVs are not thought to enter the blood stream, having an HPV infection in one part of the body should not cause an infection in another part of the body.

Once an HPV enters an epithelial cell, the virus begins to make proteins. Two of the proteins made by high-risk HPVs interfere with normal functions in the cell, enabling the cell to grow in an uncontrolled manner and to avoid cell death.

Many times these infected cells are recognized by the immune system and eliminated. Sometimes, however, these infected cells are not destroyed, and a persistent infection results. As the persistently infected cells continue to grow, they may develop mutations that promote even more cell growth, leading to the formation of a high-grade lesion and, ultimately, a tumor.

Researchers believe that it can take between 10 and 20 years from the time of an initial HPV infection until a tumor forms. However, even high-grade lesions do not always lead to cancer. The percentage of high-grade cervical lesions that progress to invasive cervical cancer has been estimated to be 50 percent or less (<u>11</u>).

Cervical Cancer



Cancer is a disease in which cells in the body grow out of control. Cancer is always named for the part of the body where it starts, even if it spreads to other body parts later.

When cancer starts in the cervix, it is called cervical cancer. The cervix is the lower, narrow end of the uterus. The cervix connects the vagina (birth canal) to the upper part of the uterus. The uterus (or womb) is where a baby grows when a woman is pregnant.

Cervical cancer is highly preventable in most Western countries because <u>screening tests</u> and a <u>vaccine</u> to prevent HPV infections are available. When cervical cancer is found early, it is highly treatable and associated with long survival and good quality of life.

Learn more by reading <u>Basic Information About Cervical Cancer</u>, downloading the *Inside Knowledge* campaign's <u>cervical cancer fact sheet</u>, <u>[PDF-874KB]</u> or listening to the <u>cervical cancer podcast</u>.

Who Gets Cervical Cancer?

All women are at risk for cervical cancer. It occurs most often in women over age 30. Each year, about 12,000 women in the United States get cervical cancer.[†]

The <u>human papillomavirus (HPV)</u> is the main <u>cause of cervical cancer</u>. HPV is a common virus that is passed from one person to another during sex. At least half of sexually active people will have HPV at some point in their lives, but few women will get cervical cancer.

†Source: U.S. Cancer Statistics Working Group. <u>United States Cancer Statistics: 1999–2010 Incidence and Mortality Web-based Report.</u> Atlanta (GA): Department of Health and Human Services, Centers for Disease Control and Prevention, and National Cancer Institute; 2013. Available at: <u>http://www.cdc.gov/uscs.</u>

Cervical Cancer Risk Factors

Almost all <u>cervical cancers are caused by human papillomavirus (HPV)</u>, a common virus that can be passed from one person to another during sex. There are many types of HPV. Some HPV types can cause changes on a woman's cervix that can lead to cervical cancer over time, while other types can cause genital or skin warts.

<u>HPV</u> is so common that most people get it at some time in their lives. HPV usually causes no symptoms so you can't tell that you have it. For most women, HPV will go away on its own; however, if it does not, there is a chance that over time it may cause cervical cancer.

Other things can increase your risk of cervical cancer-

- <u>Smoking.</u>
- Having <u>HIV</u> (the virus that causes AIDS) or another condition that makes it hard for your body to fight off health problems.
- Using birth control pills for a long time (five or more years).
- Having given birth to three or more children.
- Having several sexual partners.

Cervical Cancer Prevention

Two tests can help prevent cervical cancer-

- 1. The <u>Pap test</u> (or Pap smear) looks for precancers, cell changes on the cervix that may become cervical cancer if they are not treated appropriately. You should start getting Pap tests at age 21.
- 2. The human papillomavirus (HPV) test looks for the virus that can cause these cell changes.

The most important thing you can do to help prevent cervical cancer is to have regular screening tests starting at age 21.

If your <u>Pap test results</u> are normal, your chance of getting cervical cancer in the next few years is very low. For that reason, your doctor may tell you that you will not need another Pap test for as long as three years. If you are 30 years old or older, you may choose to have an HPV test along with the Pap test. If <u>both test results</u> are normal, your doctor may tell you that you can wait five years to have your next Pap test. But you should still go to the doctor regularly for a checkup.

For women aged 21–65, it is important to continue getting a Pap test as directed by your doctor—even if you think you are too old to have a child or are not having sex anymore. However, if you are older than 65 and have had normal Pap test results for several years, or if you have had your cervix removed as part of a total hysterectomy for a non-

cancerous condition, like fibroids, your doctor may tell you that you do not need to have a Pap test anymore.

Getting an HPV Vaccine

Two <u>HPV vaccines</u> are available to protect females against the types of HPV that cause most cervical, vaginal, and vulvar cancers. Both vaccines are recommended for 11- and 12-year-old girls, and for females 13 through 26 years of age who did not get any or all of the shots when they were younger. These vaccines also can be given to girls as young as 9 years of age. It is recommended that females get the same vaccine brand for all three doses, whenever possible. It is important to note that women who are vaccinated against HPV still need to have regular Pap tests to screen for cervical cancer.

More Steps to Help Prevent Cervical Cancer

These things may also help lower your risk for cervical cancer-

- Don't smoke.
- Use condoms during sex.*
- Limit your number of sexual partners.

*HPV infection can occur in both male and female genital areas that are covered or protected by a latex condom, as well as in areas that are not covered. While the effect of condoms in preventing HPV infection is unknown, condom use has been associated with a lower rate of cervical cancer.

Symptoms of Cervical Cancer

Early on, cervical cancer may not cause signs and symptoms. Advanced cervical cancer may cause bleeding or discharge from the vagina that is not normal for you, such as bleeding after sex. If you have any of these signs, see your doctor. They may be caused by something other than cancer, but the only way to know is to see your doctor.

Gynecologic Cancer Symptoms					
Symptoms	Cervical Cancer	Ovarian Cancer	Uterine Cancer	Vaginal Cancer	Vulvar Cancer
Abnormal vaginal bleeding or discharge					
Pelvic pain or pressure		•	•		•
Abdominal or back pain		•			
Bloating		•			
Changes in bathroom habits		•		•	
Itching or burning of the vulva					
Changes in vulva color or skin, such as a rash, sores, or warts					•

Cervical Cancer Screening

On This Page

- When to Get Screened
- <u>How to Prepare for Your Pap Test</u>
- Pap Test Results
- Screening Guidelines

Cervical cancer is the easiest female cancer to prevent, with regular screening tests and follow-up. Two screening tests can help prevent cervical cancer or find it early—

- The Pap test (or Pap smear) looks for *precancers*, cell changes on the cervix that might become cervical cancer if they are not treated appropriately.
- The HPV test looks for the virus (<u>human papillomavirus</u>) that can cause these cell changes.

The Pap test is recommended for all women between the ages of 21 and 65 years old, and can be done in a doctor's office or clinic. During the Pap test, the doctor will use a plastic or metal instrument, called a *speculum*, to widen your vagina. This helps the doctor examine the vagina and the cervix, and collect a few cells and mucus from the cervix and the area around it. The cells are then placed on a slide or in a bottle of liquid and sent to a laboratory. The laboratory will check to be sure that the cells are normal.

If you get the HPV test along with the Pap test, the cells collected during the Pap test will be tested for HPV at the laboratory. Talk with your doctor, nurse, or other health care professional about whether the HPV test is right for you.

When you have a Pap test, the doctor may also perform a pelvic exam, checking your uterus, ovaries, and other organs to make sure there are no problems. There are times when your doctor may perform a pelvic exam without giving you a Pap test. Ask your doctor which tests you are having, if you are unsure.

If you have a low income or do not have health insurance, you may be able to get a free or low-cost Pap test through the National Breast and Cervical Cancer Early Detection Program. Find out if you qualify.

When to Get Screened

You should start getting regular Pap tests at age 21. The Pap test, which screens for cervical cancer, is one of the most reliable and effective cancer screening tests available.

The only cancer for which the Pap test screens is cervical cancer. It does **not** screen for ovarian, uterine, vaginal, or vulvar cancers. So even if you have a Pap test regularly, if you notice any <u>signs or symptoms</u> that are unusual for you, see a doctor to find out why you're having them. If your Pap test results are normal, your doctor may tell you that you can wait three years until your next Pap test.

Cervical Cancer Screening with the HPV Test and the Pap Test in Women Ages 30 and Older



If you are 30 years old or older, you may choose to have an HPV test along with the Pap test. Both tests can be performed by your

doctor at the same time. When both tests are performed together, it is called *co-testing*. If your test results are normal, your chance of getting cervical cancer in the next few years

is very low. Your doctor may then tell you that you can wait as long as five years for your next screening. But you should still go to the doctor regularly for a checkup.

If you are 21–65 years old, it is important for you to continue getting a Pap test as directed by your doctor—even if you think you are too old to have a child or are not having sex anymore. If you are older than 65 and have had normal Pap test results for several years, or if you have had your cervix removed as part of a total hysterectomy for non-cancerous conditions, like fibroids, your doctor may tell you that you do not need to have a Pap test anymore.

For more information, please read the <u>U.S. Preventive Services Task Force overview</u> of cervical cancer screening recommendations.

How to Prepare for Your Pap Test

You should not schedule your Pap test for a time when you are having your period. If you are going to have a Pap test in the next two days—

- You should not douche (rinse the vagina with water or another fluid).
- You should not use a tampon.
- You should not have sex.
- You should not use a birth control foam, cream, or jelly.
- You should not use a medicine or cream in your vagina.

Pap Test Results

It can take as long as three weeks to receive your <u>Pap test results</u>. If your test shows that something might not be normal, your doctor will contact you and figure out how best to follow up. There are many reasons why Pap test results might not be normal. It usually does not mean you have cancer.

If your Pap test results show cells that are not normal and may become cancer, your doctor will let you know if you need to be treated. In most cases, treatment prevents cervical cancer from developing. It is important to follow up with your doctor right away to learn more about your test results and receive any treatment that may be needed.

Cervical Cancer Screening Guidelines

The <u>Cervical Cancer Screening Guidelines chart</u> [PDF-62KB] compares recommendations from the <u>American Cancer Society</u>, [PDF-62KB] compares Force, [P] and the <u>American College of Obstetricians and Gynecologists</u> [PDF-62KB] regarding—

- When to start screening.
- Screening methods and intervals.
- When to stop screening.
- Screening after a total hysterectomy.

- Pelvic exams.
- Screening among women who have been vaccinated against human papillomavirus (HPV).

Cervical Cancer Diagnosis and Treatment

On This Page

- <u>Types of Treatment</u>
- <u>Clinical Trials</u>
- <u>Complementary and Alternative Medicine</u>

If your doctor says that you have cervical cancer, ask to be referred to a gynecologic oncologist—a doctor who has been trained to treat cancers of a woman's reproductive system. This doctor will work with you to create a treatment plan.

The extent of disease is referred to as the stage. Information about the size of the cancer or how far it has spread is often used to determine the stage. Doctors use this information to plan treatment and to monitor progress.

For more information about stages of cervical cancer, visit the <u>National Cancer Institute</u> (NCI).

Types of Treatment

There are several ways to treat cervical cancer. The treatment depends on the type of cervical cancer and how far it has spread. Treatments include surgery, chemotherapy, and/or radiation therapy.

- Surgery: Doctors remove cancer tissue in an operation.
- **Chemotherapy:** Chemotherapy involves the use of drugs to stop or slow the growth of cancer cells. Chemotherapy may cause side effects, but these often get better or go away when chemotherapy is over. Chemotherapy drugs may be given in several forms, including pills or through an IV (intravenous) injection.
- **Radiation therapy:** Radiation therapy uses high-energy rays (similar to X-rays) to try to kill the cancer cells and stop them from spreading. The rays are aimed at the part of the body where the cancer is.

Different treatments may be provided by different doctors on your medical team.

- Gynecologic oncologists are doctors who have been trained to treat cancers of a woman's reproductive system.
- Surgeons are doctors who perform operations.
- Medical oncologists are doctors who are experts in cancer and treat cancers with medicines.
- Radiation oncologists are doctors who treat cancers with radiation.

Visit NCI for more information about treatments for cervical cancer.

Clinical Trials

Clinical trials use new treatment options to see if they are safe and effective. If you have cancer, you may want to take part. Visit the sites listed below for more information.

- <u>NIH Clinical Research Trials and You</u> (National Institutes of Health)
- Learn About Clinical Trials (National Cancer Institute)
- <u>Search for Clinical Trials</u> (National Cancer Institute)
- <u>ClinicalTrials.gov</u> (National Institutes of Health)

Complementary and Alternative Medicine

<u>Complementary and alternative medicine</u> are medicines and health practices that are not standard cancer treatments. Complementary medicine is used *in addition to* standard treatments, and alternative medicine is used *instead of* standard treatments. Meditation, yoga, and supplements like vitamins and herbs are some examples.

Many kinds of complementary and alternative medicine have not been tested scientifically and may not be safe. <u>Talk to your doctor</u> before you start any kind of complementary or alternative medicine.

Which Treatment Is Right for Me?

Choosing the treatment that is right for you may be hard. Talk to your cancer doctor about the treatment options available for your type and stage of cancer. Your doctor can explain the risks and benefits of each treatment and their side effects.

Sometimes people get an opinion from more than one cancer doctor. This is called a "second opinion." Getting a <u>second opinion</u> may help you choose the treatment that is right for you.