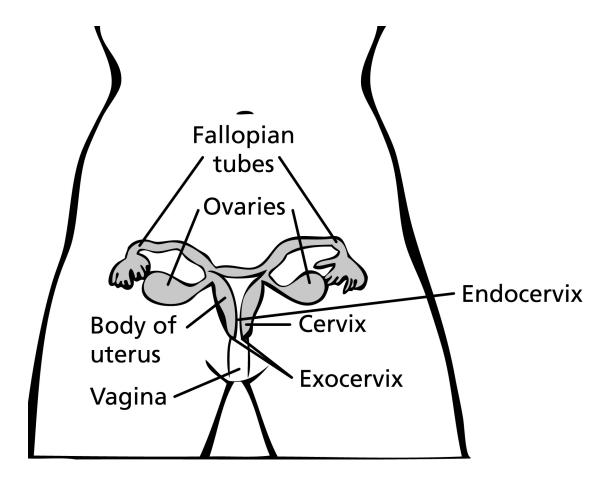


Cervical Cancer Prevention and Early Detection

What is cervical cancer?

Cervical cancer starts in cells lining the cervix. The cervix is the lower part of the uterus (womb). It is sometimes called the *uterine cervix*. The body of the uterus (the upper part) is where a fetus grows. The cervix connects the body of the uterus to the vagina (birth canal). The part of the cervix closest to the body of the uterus is called the *endocervix*. The part next to the vagina is the *exocervix* (or *ectocervix*). The 2 main types of cells covering the cervix are squamous cells (on the exocervix) and glandular cells (on the endocervix). The place these cell types meet is called the *transformation zone*. The exact location of the transformation zone changes as you age and with childbirth. Most cervical cancers start in the cells in the transformation zone.



These cells do not suddenly change into cancer. Instead, the normal cells of the cervix gradually develop pre-cancerous changes that turn into cancer. Doctors use several terms to describe these pre-cancerous changes, including cervical intraepithelial neoplasia (CIN), squamous intraepithelial lesion (SIL), and dysplasia. These changes can be detected by the Pap test and treated to prevent cancer from developing (see the sections, "The Pap (Papanicolaou) test" and "Work-up of abnormal Pap test results.").

Cervical cancers and cervical pre-cancers are classified by how they look under a microscope. There are 2 main types of cervical cancer: *squamous cell carcinoma* and *adenocarcinoma*. About 80% to 90% of cervical cancers are squamous cell carcinomas. These cancers form from cells in the exocervix, and the cancer cells have features of squamous cells under the microscope.

Most of the remaining types of cervical cancers are adenocarcinomas. Adenocarcinomas are cancers that develop from gland cells. Cervical adenocarcinoma develops from the mucus-producing gland cells of the endocervix. Cervical adenocarcinomas seem to have become more common in the last 20 to 30 years.

Less commonly, cervical cancers have features of both squamous cell carcinomas and adenocarcinomas. These are called *adenosquamous carcinomas* or *mixed carcinomas*.

Although cervical cancers start from cells with pre-cancerous changes (pre-cancers), only some women with pre-cancers of the cervix will develop cancer. The change from pre-cancer to cancer

usually takes several years – but it can happen in less than a year. For most women, precancerous cells will remain unchanged or even go away without any treatment. Still, in some women pre-cancers turn into true (invasive) cancers. Treating all pre-cancers can prevent almost all true cancers. Pre-cancerous changes are discussed in the section "Work-up of abnormal Pap test results" and treatment of pre-cancers is discussed in the section, "How women with abnormal Pap test results or pre-cancers are treated."

What are the risk factors for cervical cancer?

A risk factor is anything that changes your chance of getting a disease such as cancer. Different cancers have different risk factors. For example, exposing skin to strong sunlight is a risk factor for skin cancer. Smoking is a risk factor for many cancers. But having a risk factor, or even several, does not mean that you will get the disease.

Several risk factors increase your chance of getting cervical cancer. Women without any of these risk factors rarely develop cervical cancer. Although these factors increase the odds of getting cervical cancer, many women with these risk factors do not develop this disease.

In thinking about the following risk factors, it helps to focus on those you can change or avoid (like smoking or human papilloma virus infection), rather than those that you cannot (such as your age and family history). It's still important, though, to know about risk factors that cannot be changed, because it's even more important for women who have these factors to get regular Pap tests to detect cervical cancer early. Cervical cancer risk factors include:

Human papilloma virus infection

The most important risk factor for cervical cancer is infection by the human papilloma virus (HPV). HPV is a group of more than 150 related viruses, some of which cause a type of growth called *papillomas*, which are more commonly known as *warts*.

HPV can infect cells on the surface of the skin, and those lining the genitals, anus, mouth and throat, but not the blood or internal organs such as the heart or lungs.

HPV can be spread from one person to another during skin-to-skin contact. One way HPV is spread is through sex, including vaginal, anal, and even oral sex.

Different types of HPV cause warts on different parts of the body. Some types cause common warts on the hands and feet. Other types tend to cause warts on the lips or tongue.

Certain types of HPV may cause warts to appear on or around the genital organs and in the anal area. These warts may barely be visible or they may be several inches across. These are known as *genital warts* or *condyloma acuminatum*. HPV 6 and HPV 11 are the 2 types of HPV that cause most cases of genital warts. These are called *low-risk* types of HPV because they are seldom linked to cervical cancer.

Other types of HPV are called *high-risk types* because they are strongly linked to cancers, including cancers of the cervix, vulva, and vagina in women, penile cancer in men, and anal and oral cancer in men and women. The high-risk types include HPV 16, HPV 18, HPV 31, HPV 33,

and HPV 45, as well as some others. There might be no visible signs of infection with a high-risk HPV until pre-cancerous changes or cancer develops.

Doctors believe that a woman must be infected by HPV before she develops cervical cancer. Although this can mean infection with any of the high-risk types, about two-thirds of all cervical cancers are caused by HPV 16 and 18.

Infection with HPV is common, and in most people the body is able to clear the infection on its own. Sometimes, however, the infection does not go away and becomes chronic. Chronic infection, especially when it is with high-risk HPV types, can eventually cause certain cancers, such as cervical cancer.

Although HPV can be spread during sex – including vaginal intercourse, anal intercourse, and oral sex – sex doesn't have to occur for the infection to spread. All that is needed to pass HPV from one person to another is skin-to-skin contact with an area of the body infected with HPV. Infection with HPV seems to be able to be spread from one part of the body to another – for example, infection may start in the cervix and then spread to the vagina.

Completely avoiding putting the areas of your body that can become infected with HPV (like the mouth, anus, and genitals) in contact with those of another person <u>may</u> be the only way to truly prevent these areas from becoming infected with HPV.

The Pap test looks for changes in cervical cells caused by HPV infection. Other tests look for the infections themselves by finding genes (DNA) from HPV in the cells. For some women, the HPV test is used along with the Pap test as a part of screening. The HPV test may also be used to help decide what to do when a woman has a mildly abnormal Pap test result. If the test finds a high-risk type of HPV, it could mean she will need a full evaluation with a colposcopy procedure. Although there is currently no cure for HPV infection, there are ways to treat the warts and abnormal cell growth that HPV causes.

For more information on preventing HPV infection, see the "Can cervical cancer be prevented?" section in this document or ask for our documents called *HPV Vaccines* and *HPV and HPV Testing*.

Although scientists believe that it's necessary to have had HPV for cervical cancer to develop, most women with this virus do not develop cancer. Doctors believe that other factors must come into play for cancer to develop. Some of these known factors are listed below.

Smoking

Women who smoke are about twice as likely as non-smokers to get cervical cancer. Smoking exposes the body to many cancer-causing chemicals that affect organs other than the lungs. These harmful substances are absorbed through the lungs and carried in the bloodstream throughout the body. Tobacco by-products have been found in the cervical mucus of women who smoke. Researchers believe that these substances damage the DNA of cervix cells, and may contribute to the development of cervical cancer. Smoking also makes the immune system less effective in fighting HPV infections.

Immunosuppression

Human immunodeficiency virus (HIV), the virus that causes AIDS, damages the immune system and puts women at higher risk for HPV infection. This might, in part, explain the increased risk of cervical cancer in women with AIDS. Also, that the immune system may be important in destroying cancer cells and slowing their growth and spread. In women with an impaired immune system from HIV, a cervical pre-cancer might develop into an invasive cancer faster than it normally would. Another group of women at risk of cervical cancer are those taking drugs to suppress their immune response, such as those being treated for an autoimmune disease (in which the immune system sees the body's own tissues as foreign and attacks them, as it would a germ) or those who have had an organ transplant.

Chlamydia infection

Chlamydia is a relatively common kind of bacteria that can infect the reproductive system. It's spread by sexual contact. Chlamydia infection can cause pelvic inflammation, leading to infertility. Some studies have seen a higher risk of cervical cancer in women whose blood test results show signs of past or current chlamydia infection (compared with women with normal test results). Women who are infected with chlamydia often have no symptoms. In fact, they may not know that they are infected at all unless they are tested for chlamydia during a pelvic exam.

A diet low in fruits and vegetables

Women whose diets don't include enough fruits and vegetables may be at increased risk for cervical cancer.

Being overweight

Overweight women are more likely to develop adenocarcinoma of the cervix.

Long-term use of oral contraceptives (birth control pills)

There is evidence that taking oral contraceptives (OCs) for a long time increases the risk of cancer of the cervix. Research suggests that the risk of cervical cancer goes up the longer a woman takes OCs, but the risk goes back down again after the OCs are stopped. In one study, the risk of cervical cancer was doubled in women who took birth control pills longer than 5 years, but the risk returned to normal 10 years after they were stopped.

The American Cancer Society believes that a woman and her doctor should discuss whether the benefits of using OCs outweigh this very slight potential risk. A woman with multiple sexual partners should use condoms to lower her risk of sexually transmitted infections no matter what other form of contraception she uses.

Intrauterine device use

A study found that women who had ever used an intrauterine device (IUD) had a lower risk of cervical cancer. The effect on risk was seen even in women who had an IUD for less than a year, and the protective effect remained after the IUDs were removed.

Using an IUD might also lower the risk of endometrial (uterine) cancer. However, IUDs do have some risks. A woman interested in using an IUD should first discuss the potential risks and benefits with her doctor. Also, a woman with multiple sexual partners should use condoms to lower her risk of sexually transmitted illnesses no matter what other form of contraception she uses.

Having multiple full-term pregnancies

Women who have had 3 or more full-term pregnancies have an increased risk of developing cervical cancer. No one really knows why this is true. One theory is that these women had to have had unprotected intercourse to get pregnant, so they may have had more exposure to HPV. Also, studies have pointed to hormonal changes during pregnancy as possibly making women more susceptible to HPV infection or cancer growth. Another thought is that pregnant women might have weaker immune systems, allowing for HPV infection and cancer growth.

Being younger than 17 at your first full-term pregnancy

Women who were younger than 17 years when they had their first full-term pregnancy are almost 2 times more likely to get cervical cancer later in life than women who waited to get pregnant until they were 25 years or older.

Poverty

Poverty is also a risk factor for cervical cancer. Many women with low incomes do not have ready access to adequate health care services, including Pap tests. This means they might not get screened or treated for cervical cancers and pre-cancers.

Diethylstilbestrol (DES)

DES is a hormonal drug that was given to some women to prevent miscarriage between 1940 and 1971. Women whose mothers took DES when pregnant with them are often called *DES daughters*. These women develop clear cell adenocarcinoma of the vagina or cervix more often than would normally be expected. This type of cancer is extremely rare in women who are not DES daughters. There is about 1 case of this type of cancer in every 1,000 women whose mother took DES during their pregnancy. This means that about 99.9% of DES daughters do not develop these cancers.

DES-related clear cell adenocarcinoma is more common in the vagina than the cervix. The risk appears to be greatest in women whose mothers took the drug during their first 16 weeks of pregnancy. The average age of women when they are diagnosed with DES-related clear-cell

adenocarcinoma is 19 years. Since the use of DES during pregnancy was stopped by the FDA in 1971, even the youngest DES daughters are older than 35 – past the age of highest risk. Still, there's no age cut-off when these women are safe from DES-related cancer. Doctors do not know exactly how long women will remain at risk.

DES daughters may also be at increased risk of developing squamous cell cancers and precancers of the cervix linked to HPV.

Although DES daughters have an increased risk of developing clear cell carcinomas, women don't have to be exposed to DES for clear cell carcinoma to develop. It is extremely rare, but women were diagnosed with the disease before DES was invented.

You can learn more about DES in our separate document called *DES Exposure: Questions and Answers*. It can be read on our website, or call to have a free copy sent to you.

Having a family history of cervical cancer

Cervical cancer may run in some families. If a woman's mother or sister had cervical cancer, her chances of developing the disease are 2 to 3 times higher than if no one in the family had it. Some researchers suspect some instances of this familial tendency are caused by an inherited condition that makes some women less able to fight off HPV infection than others. In other instances, women from the same family as a patient already diagnosed could be more likely to have one or more of the other non-genetic risk factors previously described in this section.

Signs and symptoms of cervical cancer

Women with early cervical cancers and pre-cancers usually have no symptoms. Symptoms often do not begin until a pre-cancer becomes a true invasive cancer and grows into nearby tissue. When this happens, the most common symptoms are:

- Abnormal vaginal bleeding, such as bleeding after sex (vaginal intercourse), bleeding after menopause, bleeding and spotting between periods, and having longer or heavier (menstrual) periods than usual. Bleeding after douching, or after a pelvic exam is a common symptom of cervical cancer but not pre-cancer.
- An unusual discharge from the vagina the discharge may contain some blood and may occur between your periods or after menopause.
- Pain during sex (vaginal intercourse).

These signs and symptoms can also be caused by conditions other than cervical cancer. For example, an infection can cause pain or bleeding. Still, if you have any of these problems, you should see your health care professional right away – even if you have been getting regular Pap tests. If it is an infection, it will need to be treated. If it's cancer, ignoring symptoms might allow it to progress to a more advanced stage and lower your chance for effective treatment.

Even better, don't wait for symptoms to appear. Be screened regularly.

Can cervical cancer be prevented?

Since the most common form of cervical cancer starts with pre-cancerous changes, there are 2 ways to stop this disease from developing. One way is to find and treat pre-cancers before they become true cancers, and the other is to prevent the pre-cancers in the first place.

Finding cervical pre-cancers

A well-proven way to prevent cervix cancer is to have testing (screening) to find pre-cancers before they can turn into invasive cancer. The Pap test (sometimes called the *Pap smear*) and the HPV (human papilloma virus) test are used for this. If a pre-cancer is found, it can be treated, stopping cervical cancer before it really starts. Since no HPV vaccine provides complete protection against all of the HPV types that can cause cancer of the cervix, it cannot prevent all cases of cervical cancer. This is why it is very important that women continue to have cervical cancer screening even after they've been vaccinated. Most invasive cervical cancers are found in women who have not had regular screening.

See the section, "The American Cancer Society guidelines for the prevention and early detection of cervical cancer" for more details.

Things to do to prevent pre-cancers and cancers

Avoid contact with the human papilloma virus (HPV)

Since HPV is the main cause of cervical cancer and pre-cancer, avoiding exposure to HPV could help you prevent this disease. HPV is passed from one person to another during skin-to-skin contact with an infected area of the body. Although HPV can be spread during sex – including vaginal, anal, and oral sex – sex doesn't have to occur for the infection to spread. All that is needed is skin-to-skin contact with an area of the body infected with HPV. This means that the virus can be spread through genital-to-genital contact (without intercourse). It is even possible for a genital infection to spread through hand-to-genital contact.

Also, HPV infection seems to be able to be spread from one part of the body to another. This means that an infection may start in the cervix and then spread to the vagina and vulva.

It can be very hard not to be exposed to HPV. It **may** be possible to prevent genital HPV infection by not allowing others to have contact with your anal or genital area, but even then there might be other ways to become infected that aren't yet clear. For example, a recent study found HPV on the surface of sex toys, so sharing sex toys might spread HPV.

HPV infection in women: HPV infections occur mainly in younger women and are less common in women older than 30. The reason for this is not clear. Certain types of sexual behavior increase a woman's risk of getting HPV infection, such as having sex at an early age and having many sex partners.

Women who have had many sex partners are more likely to get infected with HPV, but a woman who has had only one sex partner can still get infected. This is more likely if she has a partner who has had many sex partners or if her partner is an uncircumcised male.

Waiting to have sex until you are older can help you avoid HPV. It also helps to limit your number of sex partners and to avoid having sex with someone who has had many other sex partners. Although the virus most often spreads between a man and a woman, HPV infection and cervical cancer also are seen in women who have only had sex with other women. Remember that someone can have HPV for years and still have no symptoms – it does not always cause warts or other problems. Someone can have the virus and pass it on without knowing it.

Still, since all that's needed to pass HPV from one person to another is skin-to-skin contact with an area of the body infected with HPV, even never having sex doesn't guarantee that you won't ever get infected. It might be possible to prevent anal and genital HPV infection by never allowing another person to have contact with those areas of your body.

HPV infection in men: For men, the main factors influencing the risk of genital HPV infection are circumcision and the number of sex partners.

Men who are circumcised (have had the foreskin of the penis removed) have a lower chance of becoming and staying infected with HPV. Men who have **not** been circumcised are more likely to be infected with HPV and pass it on to their partners. The reasons for this are unclear. It may be that after circumcision the skin on the glans (of the penis) goes through changes that make it more resistant to HPV infection. Another theory is that the surface of the foreskin (which is removed by circumcision) is more easily infected by HPV. Still, circumcision does not completely protect against HPV infection – men who are circumcised can still get HPV and pass it on to their partners.

The risk of being infected with HPV is also strongly linked to having many sexual partners (over a man's lifetime).

Use condoms

Condoms ("rubbers") provide some protection against HPV but they don't completely prevent infection. Men who use condoms are less likely to be infected with HPV and to pass it on to their female partners. One study found that when condoms are used correctly every time sex occurs they can lower the HPV infection rate by about 70%. One reason that condoms cannot protect completely is because they don't cover every possible HPV-infected area of the body, such as skin of the genital or anal area. Still, condoms provide some protection against HPV, and they also protect against HIV and some other sexually transmitted infections. Condoms (when used by the male partner) also seem to help the HPV infection and cervical pre-cancers go away faster.

Female condoms fit inside the vagina and can help protect against pregnancy. They also can protect against sexually transmitted infections, including HPV and HIV, although for this they aren't as effective as male condoms.

Don't smoke

Not smoking is another important way to reduce the risk of cervical pre-cancer and cancer.

Get vaccinated

Vaccines are available that can protect against certain HPV infections. All of these vaccines protect against infection with HPV subtypes 16 and 18. Some can also protect against infections with other HPV subtypes, including some types that cause anal and genital warts.

These vaccines only work to prevent HPV infection – they will not treat an infection that is already there. That is why, to be most effective, the HPV vaccines should be given before a person becomes exposed to HPV (such as through sexual activity).

These vaccines help prevent pre-cancers and cancers of the cervix. Some HPV vaccines are also approved to help prevent other types of cancers and anal and genital warts.

The vaccines require a series of 3 injections over a 6-month period. Side effects are usually mild. The most common one is short-term redness, swelling, and soreness at the injection site. Rarely, a young woman will faint shortly after the vaccine injection.

The Federal Advisory Committee on Immunization Practices (ACIP) recommends that females aged 11 to 12 routinely be vaccinated for HPV with the full series of 3 shots. Females as young as age 9 may also receive the HPV vaccine at the discretion of their doctors. ACIP also recommended women ages 13 to 26 who have not yet been vaccinated get "catch-up" vaccinations.

The American Cancer Society also recommends that the HPV vaccine be routinely given to girls ages 11 to 12 and as early as age 9 at the discretion of doctors. The Society also agrees that "catch-up" vaccinations should be given to females up to age 18. The independent panel making the Society recommendations found that there was not yet enough proof that catch-up vaccinations for all women aged 19 to 26 years would be beneficial. As a result, the American Cancer Society recommends that women aged 19 to 26 talk with their health care provider about their risk of previous HPV exposure and potential benefit from vaccination before deciding to get the vaccine. At this time, the American Cancer Society's guidelines do not address the use of the vaccine in older women or males.

It's important to realize that no vaccine provides complete protection against all cancer-causing types of HPV, so routine cervical cancer screening is still necessary.

For more information on the vaccine and HPV, please see our document, HPV Vaccines.

The American Cancer Society guidelines for the prevention and early detection of cervical cancer

The American Cancer Society recommends that women follow these guidelines to help find cervical cancer early. Following these guidelines can also find pre-cancers, which can be treated to keep cervical cancer from forming.

- All women should begin cervical cancer testing (screening) at age 21. Women aged 21 to 29, should have a Pap test every 3 years. HPV testing should not be used for screening in this age group (it may be used as a part of follow-up for an abnormal Pap test).
- Beginning at age 30, the preferred way to screen is with a Pap test combined with an HPV test every 5 years. This is called co-testing and should continue until age 65.
- Another reasonable option for women 30 to 65 is to get tested every 3 years with just the Pap test.
- Women who are at high risk of cervical cancer because of a suppressed immune system (for example from HIV infection, organ transplant, or long term steroid use) or because they were exposed to DES in utero may need to be screened more often. They should follow the recommendations of their health care team.
- Women over 65 years of age who have had regular screening in the previous 10 years should stop cervical cancer screening as long as they haven't had any serious pre-cancers (like CIN2 or CIN3) found in the last 20 years (CIN stands for cervical intraepithelial neoplasia and is discussed later in the section "Work-up of an abnormal Pap test result" under the heading "How biopsy results are reported"). Women with a history of CIN2 or CIN3 should continue to have testing for at least 20 years after the abnormality was found.
- Women who have had a total hysterectomy (removal of the uterus and cervix) should stop screening (such as Pap tests and HPV tests), unless the hysterectomy was done as a treatment for cervical pre-cancer (or cancer). Women 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.
- Women of any age should NOT be screened every year by any screening method
- Women who have been vaccinated against HPV should still follow these guidelines.

Some women believe that they can stop cervical cancer screening once they have stopped having children. This is not true. They should continue to follow American Cancer Society guidelines.

Although annual (every year) screening should not be done, women who have abnormal screening results may need to have a follow-up Pap test (sometimes with a HPV test) done in 6 months or a year.

The American Cancer Society guidelines for early detection of cervical cancer do not apply to women who have been diagnosed with cervical cancer, cervical pre-cancer, or HIV infection. These women should have follow-up testing and cervical cancer screening as recommended by their healthcare team.

Importance of being screened for cervical cancer

Screening tests offer the best chance to have cervical cancer found at an early stage when successful treatment is likely. Screening can also actually prevent most cervical cancers by

finding abnormal cervix cell changes (pre-cancers) so that they can be treated before they have a chance to turn into a cervical cancer.

If it's detected early, cervical cancer is one of the most successfully treatable cancers. In the United States, the cervical cancer death rate declined by more than 50% over the last 30 years. This is thought to be mainly due to the effectiveness of Pap test screening.

Despite the recognized benefits of cervical cancer screening, not all American women take advantage of it. Most cervical cancers are found in women who have never had a Pap test or who have not had one recently. Women without health insurance and women who have recently immigrated are less likely to have timely cervical cancer screening.

Cervical cancer deaths are higher in populations around the world where women do not have routine cervical cancer screening. In fact, cervical cancer is the major cause of cancer deaths in women in many developing countries. These women are usually diagnosed with late stage cancers, rather than pre-cancers or early cancers.

The HPV DNA test

As mentioned earlier, the most important risk factor for developing cervical cancer is infection with HPV. Doctors can now test for the types of HPV (high-risk or carcinogenic types) that are most likely to cause cervical cancer by looking for pieces of their DNA in cervical cells. The test is done similarly to the Pap test in terms of how the sample is collected, and it sometimes can even be done on the same sample.

The HPV DNA test is most often used in 2 situations:

- The HPV gene test can be used in combination with the Pap test to screen for cervical cancer. The American Cancer Society recommends this combination for women 30 and older. In the American Cancer Society guidelines, the HPV test does not replace the Pap test for most women. The American Cancer Society does not recommend using the HPV DNA test to screen for cervical cancer in women under 30. That is because women in their 20s who are sexually active are much more likely (than older women) to have an HPV infection that will go away on its own. For these younger women, results of this test are not as significant and may be more confusing. For more information, see the American Cancer Society document HPV and HPV Testing.
- The HPV DNA test can also be used in women who have slightly abnormal Pap test results (ASC-US) to find out if they might need more testing or treatment. See the section "Work-up of abnormal Pap test results."

An HPV DNA test has been approved by the FDA to be used without a Pap test to screen for cervical cancer. At this time, the American Cancer Society is considering the evidence supporting the use of this test for screening and may issue updates to our screening guidelines in 2015.

Follow-up of HPV testing

If your Pap test result is normal, but you test positive for HPV, the main options are:

- Repeat co-testing (with a Pap test and an HPV test) in one year
- Testing to see if you test positive for HPV types 16 or 18 (this can often be done on the sample in the lab). If you are, colposcopy would be recommended (colposcopy is discussed in the section, "Work-up of abnormal Pap test results"). If you test negative, you should get repeat co-testing in one year.

The Pap (Papanicolaou) test

The Pap test is the main screening test for cervical cancer and pre-cancerous changes. A woman should know how it is done and how often they should have a Pap test.

How the Pap test is done

The Pap test is a procedure used to collect cells from the cervix so that they can be looked at under the microscope to find cancer and pre-cancer.

The health care professional first places a speculum inside the vagina. The speculum is a metal or plastic instrument that keeps the vagina open so that the cervix can be seen clearly. Next, using a small spatula, a sample of cells and mucus is lightly scraped from the exocervix. A small brush or a cotton-tipped swab is then inserted into the opening of the cervix to take a sample from the endocervix (see illustration in "What is cervical cancer?" section). If your cervix has been removed (because you had a trachelectomy or hysterectomy) as a part of the treatment for a cervical cancer or pre-cancer, the cells will be sampled from the upper part of the vagina (known as the *vaginal cuff*).

The cell samples are then prepared so that they can be examined under a microscope in the laboratory. This this is done either by:

- Smearing the sample directly onto a glass microscope slide and spraying it with a preservative. The slide is then sent to the laboratory. This is called *conventional cytology*.
- Putting the sample of cells from the cervix into a special preservative liquid (instead of putting them on a slide directly). The bottle containing the cells and the liquid is sent to the lab. The cells in the liquid are spread onto slides in the lab. This is called *liquid-based cytology*, or a *liquid-based Pap test*.

Liquid-based testing does not find more cancers or pre-cancers than conventional cytology but it does have some advantages. These include a lower chance that the Pap test will need to be repeated, and the ability to use the same sample for HPV testing. A drawback of the liquid-based test is that it is more likely to find cell changes that are not pre-cancerous but that will need to be checked out further – leading to unnecessary tests. This method is also more expensive than conventional cytology.

Although the Pap test has been more successful than any other screening test in preventing a cancer, it's not perfect. One of the limitations of the Pap test is that the results need to be examined by humans, so an accurate analysis of the hundreds of thousands of cells in each sample is not always possible. Engineers, scientists, and doctors are working together to improve this test. Because some abnormalities may be missed (even when samples are looked at in the best laboratories), it's not a good idea to have this test less often than American Cancer Society guidelines recommend. Unfortunately, many of the women most at risk for cervical cancer are not being tested often enough or at all.

Making your Pap tests more accurate

You can do several things to make your Pap test as accurate as possible:

- Try not to schedule an appointment for a time during your menstrual period. The best time is at least 5 days after your menstrual period stops.
- Don't use tampons, birth-control foams or jellies, other vaginal creams, moisturizers, or lubricants, or vaginal medicines for 2 to 3 days before the test.
- Don't douche for 2 to 3 days before the test.
- Don't have sexual intercourse for 2 days before the test.

A pelvic exam is not the same as a Pap test

Many people confuse pelvic exams with Pap tests. The pelvic exam is part of a woman's routine health care. During a pelvic exam, the doctor looks at and feels the reproductive organs, including the uterus and the ovaries and may do tests for sexually transmitted disease. Pap tests are often done during pelvic exams, but you can have a pelvic exam without having a Pap test. A pelvic exam without a Pap test will not help find abnormal cells of the cervix or cervical cancer at an early stage.

The Pap test is often done during a pelvic exam, after the speculum is placed. To do a Pap test, the doctor removes cells from the cervix by gently scraping or brushing it with a special instrument. Pelvic exams may help find other types of cancers and reproductive problems, but a Pap test is needed to find early cervical cancer or pre-cancers. Ask your doctor if you had a Pap test with your pelvic exam.

How Pap test results are reported

The most widely used system for describing Pap test results is the Bethesda System (TBS). There are 3 main categories, some of which have sub-categories:

- Negative for intraepithelial lesion or malignancy,
- Epithelial cell abnormalities
- Other malignant neoplasms.

Negative for intraepithelial lesion or malignancy

This first category means that no signs of cancer, pre-cancerous changes, or other significant abnormalities were found. Some specimens in this category appear entirely normal. Others may have findings that are unrelated to cervical cancer, such as signs of infection with yeast, herpes, or *Trichomonas vaginalis* (a microscopic parasite), for example. Specimens from some women may also show "reactive cellular changes", which is the way cervical cells respond to infection or other irritation.

Epithelial cell abnormalities

This means that the cells lining the cervix or vagina show changes that might be cancer or a precancerous condition. This category is divided into several groups for squamous cells and glandular cells.

Squamous cell abnormalities

Atypical squamous cells (ASCs): This category includes atypical squamous cells of uncertain significance (ASC-US) and atypical squamous cells where high-grade squamous intraepithelial lesion (SIL) can't be excluded (ASC-H).

ASC-US is a term used when there are cells that look abnormal, but it is not possible to tell (by looking at the cells under a microscope) if this is caused by infection, irritation, or if it is a precancer. Most of the time, cells labeled ASC-US are not pre-cancer, but more testing is needed to be sure.

If the results of a Pap test are labeled ASC-H, it means that a SIL is suspected.

Pap test results of either type of ASC mean that more testing is needed. This is discussed in the section, "Work-up of abnormal Pap test results."

Squamous intraepithelial lesions (SILs): These abnormalities are subdivided into low-grade SIL (LSIL) and high-grade SIL (HSIL). In LSIL, the cells are mildly abnormal, while in HSIL, the cells are severely abnormal. HSILs are less likely than LSILs to go away without treatment. They are also more likely to eventually develop into cancer if they are not treated. Treatment can cure most SILs and prevent true cancer from developing.

Further tests are needed if SIL is seen on a Pap test. This is discussed in the section, "Work-up of abnormal Pap test results."

Squamous cell carcinoma: This result means that the woman is likely to have an invasive cancer. Further testing will be done to be sure of the diagnosis before treatment can be planned.

Glandular cell abnormalities

Adenocarcinoma: Cancers of the glandular cells are called *adenocarcinomas*. In some cases, the pathologist examining the cells can tell whether the adenocarcinoma started in the endocervix, in the uterus (endometrium), or elsewhere in the body.

Atypical glandular cells: When the glandular cells do not look normal, but have features that do not permit a clear decision as to whether they are cancerous, the term used is *atypical glandular cells* (*AGCs*). The patient should have more testing if her cervical cytology result shows atypical glandular cells.

Other malignant neoplasms

This category is for forms of cancer that only rarely affect the cervix, such as malignant melanoma, sarcomas, and lymphoma.

Other descriptions of Pap test results have also been used in the past.

Work-up of abnormal Pap test results

Other tests for women with abnormal test results

The Pap test is a screening test – not a diagnostic test – it cannot tell for certain that cancer is present. An abnormal Pap test result means that other tests will need to be done to find out if a cancer or a pre-cancer is actually present. The tests that are used include colposcopy (with biopsy) and endocervical scraping. If a biopsy shows a pre-cancer, doctors will take steps to keep an actual cancer from developing.

Sometimes these tests are also done to follow-up a positive HPV test result when the Pap test is normal.

Colposcopy

If you have certain symptoms that suggest cancer or if your Pap test shows abnormal cells, you will need to have a test called *colposcopy*. In this procedure you will lie on the exam table as you do for a pelvic exam. A speculum will be placed in the vagina to help the doctor see the cervix. The doctor will use a colposcope to examine the cervix. The colposcope is an instrument that has magnifying lenses (like binoculars). Although it stays outside the woman's body, it lets the doctor see the surface of the cervix closely and clearly. The doctor will apply a weak solution of acetic acid (similar to vinegar) to your cervix to make any abnormal areas easier to see.

Colposcopy itself causes no more discomfort than any other speculum exam. It has no side effects, and can be done safely even if you're pregnant. Like the Pap test, it's rarely done during your menstrual period. If an abnormal area is seen on the cervix, a biopsy will be done. For a biopsy, a small piece of tissue is removed from the area that looks abnormal. The sample is sent to a pathologist to look at under a microscope. A biopsy is the only way to tell for certain if an abnormal area is a pre-cancer, a true cancer, or neither. Although the colposcopy procedure is not painful, cervical biopsy can cause discomfort, cramping, or even pain in some women.

Cervical biopsies

Several types of biopsies are used to diagnose cervical pre-cancers and cancers. If the biopsy can completely remove all of the abnormal tissue, it may be the only treatment needed. In some situations, additional treatment of pre-cancers or cancers is needed.

Colposcopic biopsy

For this type of biopsy, a doctor or other health care professional first examines the cervix with a colposcope to find the abnormal areas. Using a biopsy forceps, the doctor will remove a small (about 1/8-inch) section of the abnormal area on the surface of the cervix. The biopsy procedure may cause mild cramping or brief pain, and you may bleed lightly afterward. A local anesthetic is sometimes used to numb the cervix before the biopsy.

Endocervical curettage (endocervical scraping)

Sometimes the transformation zone (the area at risk for HPV infection and pre-cancer) cannot be seen with the colposcope. In that situation, something else must be done to check that area for cancer. This means taking a scraping of the endocervix by inserting a narrow instrument (called a *curette*) into the endocervical canal (the passage between the outer part of the cervix and the inner part of the uterus). The curette is used to scrape the inside of the canal to remove some of the tissue, which is then sent to the laboratory for examination. After this procedure, patients may feel a cramping pain, and they may also have some light bleeding. This procedure is usually done at the same time as the colposcopic biopsy.

Cone biopsy

In this procedure, also known as *conization*, the doctor removes a cone-shaped piece of tissue from the cervix. The base of the cone is formed by the exocervix (outer part of the cervix), and the point or apex of the cone is from the endocervical canal. The transformation zone (the border between the exocervix and endocervix) is contained within the cone. This is the area of the cervix where pre-cancers and cancers are most likely to develop. The cone biopsy can be used as a treatment to completely remove many pre-cancers and some very early cancers. Having a cone biopsy will not keep most women from getting pregnant, but if the biopsy removes large amount of tissue these women may have a higher risk of giving birth prematurely.

There are 2 methods commonly used for cone biopsies: the loop electrosurgical excision procedure (LEEP) (also called *large loop excision of the transformation zone* or LLETZ) and the cold knife cone biopsy.

Loop electrosurgical procedure (LEEP or LLETZ): With this method, the tissue is removed with a thin wire loop that is heated by electrical current and acts as a scalpel. For this procedure, a local anesthetic is used, and it can be done in your doctor's office. It can take as little as 10 minutes. You may have mild cramping during and after the procedure, and mild to moderate bleeding for several weeks.

Cold knife cone biopsy: This method uses a surgical scalpel or a laser instead of a heated wire to remove tissue. It requires general anesthesia (you are asleep during the operation) and is done in a hospital, but no overnight stay is needed. After the procedure, cramping and some bleeding may persist for a few weeks.

How biopsy results are reported

The terms used for reporting biopsy results are slightly different from the Bethesda System for reporting Pap test results. Pre-cancerous changes on a biopsy are called *cervical intraepithelial neoplasia* (CIN), while on a Pap test they would be called squamous intraepithelial lesion (SIL). CIN is graded on a scale of 1 to 3 based on how much of the cervical tissue looks abnormal when viewed under the microscope. In CIN1, not much of the tissue looks abnormal, and it's considered the least serious cervical pre-cancer. In CIN2 more of the tissue looks abnormal, and in CIN3 most of the tissue looks abnormal. CIN3 is the most serious pre-cancer.

Sometimes the term *dysplasia* is used instead of CIN. CIN1 is the same as mild dysplasia, CIN2 is the same as moderate dysplasia, and CIN3 includes severe dysplasia as well as carcinoma in situ.

The terms for reporting cancers (squamous cell carcinoma and adenocarcinoma) are the same for Pap tests and biopsies.

When are these tests used?

What tests (or treatment) you will need depends on the results of the Pap test.

Atypical squamous cells (ASC-US and ASC-H)

If the Pap results show atypical squamous cells of uncertain significance (ASC-US), some doctors will repeat the Pap test in 12 months. Another option is to test for human papilloma virus (HPV). What is done next depends on how old you are. If you are 21 to 24 years old, and HPV DNA is found, the doctor will recommend a repeat Pap test in a year. If you are at least 25 years old and HPV is detected, the doctor will recommend a colposcopy. If HPV is not detected, then the doctor will recommend the Pap test be repeated in 3 years. If you are at least 25 years old, an HPV test will be done at the same time as the repeat Pap test.

If the results of a Pap test are labeled atypical squamous cells cannot exclude high-grade squamous intraepithelial lesion (ASC-H), it means that a high grade SIL is suspected. The doctor will recommend colposcopy.

Squamous intraepithelial lesions (SILs)

These abnormalities are divided into low-grade SIL (LSIL) and high-grade SIL (HSIL).

For LSIL, further testing depends upon HPV testing:

- If the HPV test result was negative (meaning the virus wasn't detected), then repeating the Pap test and HPV test in one year is recommended.
- If HPV was found, then colposcopy is recommended.
- If no HPV test was done and the woman is at least 25 years old, colposcopy is recommended.
- If the woman is under 25, she should have a repeat Pap test in a year.

• Pregnant women with LSIL should have colposcopy.

For HSIL, either colposcopy or a loop electrosurgical procedure is recommended for women 25 and older. For women under 25, colposcopy is recommended.

Atypical glandular cells and adenocarcinoma in situ (on a Pap test)

If the Pap results read atypical glandular cells or adenocarcinoma but the report says that the abnormal cells do not seem to be from the lining of the uterus (the endometrium), guidelines recommend colposcopy with the biopsy type called *endocervical curettage* (endocervical scraping). The doctor may also biopsy the endometrium (this can be done at the same time as the colposcopy). For information about endometrial biopsy, see our document *Endometrial (Uterine) Cancer*.

If the atypical glandular or adenocarcinoma cells look like they are from the endometrium (based on how they look under the microscope), experts recommend a biopsy of the endometrium along with an endocervical curettage, but a colposcopy isn't needed unless the results from the endometrial biopsy are negative and do not explain the Pap test result.

How women with abnormal Pap test results or pre-cancers are treated

Treating women with abnormal Pap test results and pre-cancers can prevent cervical cancer from developing

If an abnormal area is seen during the colposcopy, your doctor will be able to remove it with a loop electrosurgical procedure (LEEP or LLETZ procedure, which were discussed in the previous section). Other options include a cone biopsy and destroying the abnormal cells with cryosurgery or laser surgery.

During cryosurgery, a metal probe cooled with liquid nitrogen is placed directly on the cervix. This kills the abnormal cells by freezing them. This can be done in a doctor's office or clinic. After cryosurgery, you may have a lot of watery brown discharge for a few weeks.

In laser surgery, a focused laser beam, directed through the vagina, is used to vaporize (burn off) abnormal cells or to remove a small piece of tissue for study. This can be done in a doctor's office or clinic and is done under local anesthesia (numbing medicine).

For a cone biopsy, a cone-shaped piece of tissue is removed from the cervix. This is done using a surgical or laser knife (cold knife cone biopsy) or using a thin wire heated by electricity (the loop electrosurgical, LEEP or LEETZ procedure). After the procedure, the tissue removed (the cone) is examined under the microscope. If the margins (outer edges) of the cone contain abnormal (cancer or pre-cancer) cells (called positive margins), some cancer (or pre-cancer) may have been left behind, so further treatment is needed.

These treatments are almost always effective in destroying pre-cancers and preventing them from developing into true cancers. You will need follow-up exams to make sure that the abnormality does not come back. If it does, the treatments can be repeated. Rarely, surgery to remove the

cervix (often with the body of the uterus) is used to treat pre-cancers. These, called trachelectomy and hysterectomy, are more often used to invasive cancers, and are discussed in our document *Cervical Cancer*.

Cervical cancer prevention and screening: Financial issues

Financial issues can play an important role in whether or not women are screened for cervical cancer. Women with lower incomes and those without health insurance are less likely to be screened.

Many states ensure that private insurance companies, Medicaid, and public employee health plans provide coverage and reimbursement for Pap test screening. The American Cancer Society supports such coverage assurances, because they remove financial barriers for women who have health insurance, but whose insurance plans previously did not cover Pap tests.

Other programs are also available to help provide financial assistance for women with lower incomes and those without insurance.

Federal law

Coverage of cervical cancer screening tests is mandated by the Affordable Care Act (ACA), but that doesn't apply to health plans that were in place before it was passed. You can find out the date your insurance plan started by contacting your health insurance plan administrator. If your plan started on or after September 23, 2010, it's required to cover the recommended cervical cancer screening tests. If your plan started before September 23, 2010, it may still have coverage requirements mandated by your state, but each state is different.

Self-insured plans

Self-insured (or self-funded) plans pay employee health care costs from their own funds, even though they usually contract with another company to track and pay claims. You can find out if your health plan is self-insured by contacting your insurance administrator at work or reading your Summary of Plan Benefits.

These plans are governed by the Affordable Care Act (ACA), so most are required to cover cervical cancer screening. The exception is any self-insured plan that was in effect before the ACA. These plans are called *grandfathered*, and they don't have to provide coverage based on what the ACA says. They also are not covered by state laws, including those about cervical cancer screening.

Women who have self-insured based health insurance should check with their health plans to see what cervical cancer screening services are offered.

Medicaid

By statute or agency policy, Medicaid or public assistance programs in all 50 states and the District of Columbia cover screening for cervical cancer either routinely or on a doctor's recommendation. This coverage may or may not conform to American Cancer Society guidelines. Please check with your state Medicaid office to learn more about what services are provided for cervical cancer screening.

Medicare

Medicare provides coverage for a screening Pap test, pelvic exam, and a clinical breast exam every 2 years for Medicare beneficiaries. And if a woman is of childbearing age and has had an abnormal Pap test in the previous 3 years, or is at high risk for cervical or vaginal cancer, she would be eligible under Medicare to be covered for screening every year. This screening is provided without co-pay, co-insurance, or deductible as long as you go to a doctor that accepts what Medicare pays as full payment (this is called accepting *assignment*). Doctors that don't accept assignment are required to tell you up front.

National Breast and Cervical Cancer Early Detection Program

All states are making cervical cancer screening more available to medically underserved women through the National Breast and Cervical Cancer Early Detection Program (NBCCEDP). This program provides breast and cervical cancer screening to women without health insurance for free or at very little cost. The NBCCEDP attempts to reach as many women in medically underserved communities as possible, including older women, women without health insurance and women who are members of racial and ethnic minorities.

Though the program is administered within each state, the Centers for Disease Control and Prevention (CDC) provides matching funds and support to each state program.

Each state's Department of Health will have information on how to contact the nearest program participant. For more information on this program, you can also contact the CDC at 1-800-CDC-INFO (1-800-232-4636) or on the web at www.cdc.gov/cancer/nbccedp.

If cervical cancer is detected during screening in this program, most states can now extend Medicaid benefits to these women to cover the costs of treatment.

You can learn more about this program in our document called *National Breast and Cervical Cancer Early Detection Program*.

HPV vaccine costs

It's expected that insurance plans will cover the cost of the HPV vaccine in accordance with the Federal Advisory Committee on Immunization Practices (ACIP) recommendations. ACIP has also recommended that the HPV vaccine be included in the federal Vaccine for Children (VFC) entitlement program, which covers vaccine costs for children and teens who don't have insurance or who are underinsured.

Additional resources

More information from your American Cancer Society

The following information may also be helpful to you. These materials may be ordered from our toll-free number, 1-800-227-2345.

American Cancer Society Recommendations for Human Papillomavirus (HPV) Vaccine Use to Prevent Cervical Cancer and Pre-Cancers

Cervical Cancer (also in Spanish)

HPV Vaccines

HPV and **HPV** Testing

What Women Should Know About Cervix Cancer and the Human Papilloma Virus (also in Spanish)

National organizations and websites*

Along with the American Cancer Society, other sources of information and support include:

Foundation for Women's Cancer (formerly Gynecologic Cancer Foundation)

Toll free number: 1-800-444-4441 or 1-312-578-1439 Website: www.foundationforwomenscancer.org

Centers for Disease Control and Prevention (CDC)

National Breast and Cervical Cancer Early Detection Program

Toll free number: 1-800-CDC-INFO (1-800-232-4636)

Website: www.cdc.gov/cancer/nbccedp

National Cervical Cancer Coalition

Toll free number: 1-800- 685-5531or 1-818-909-3849

Website: www.nccc-online.org

Planned Parenthood Federation of America

Toll-free number: 1-800-230-7526 Web site: www.plannedparenthood.org

No matter who you are, we can help. Contact us anytime, day or night, for information and support. Call us at **1-800-227-2345** or visit www.cancer.org.

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^{*}Inclusion on this list does not imply endorsement by the American Cancer Society.

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