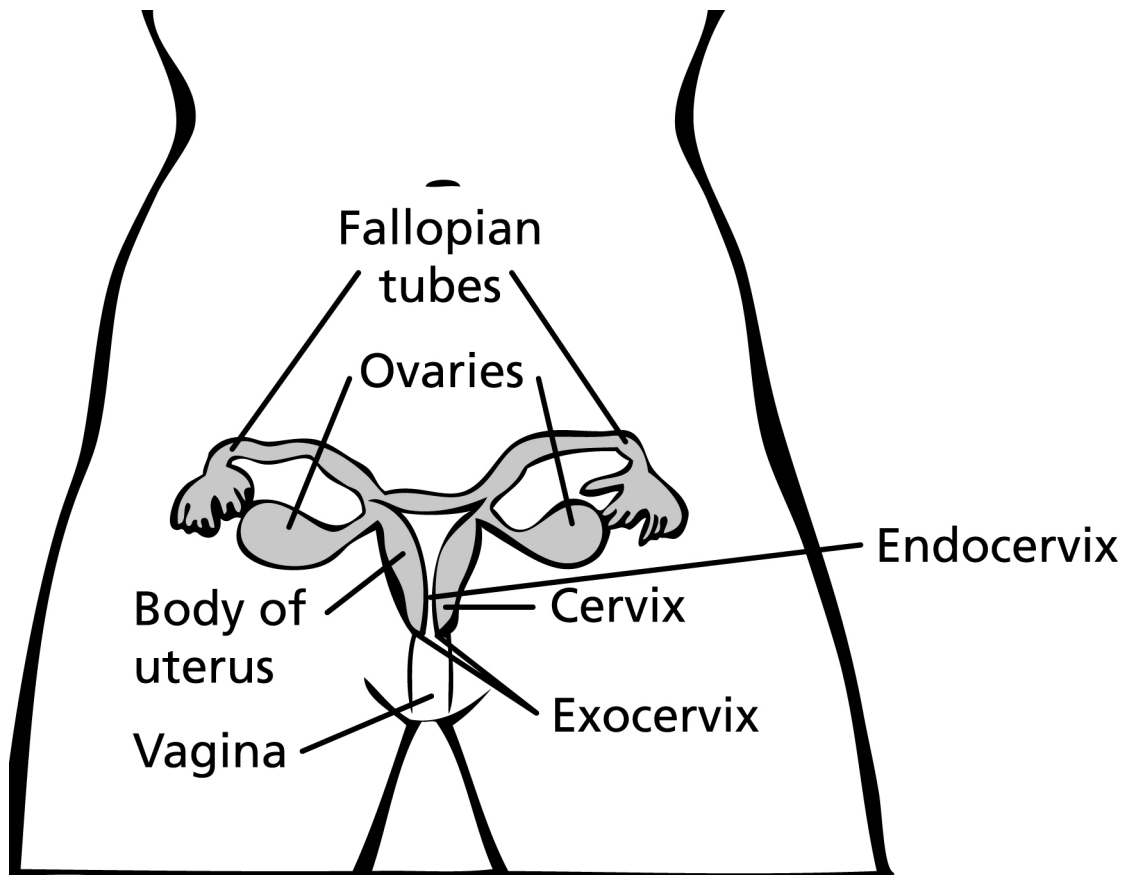




Cervical Cancer: Prevention and Early Detection

What is cervical cancer?

Cervical cancer is cancer that starts in 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 2 cell types meet is called the *transformation zone*. Most cervical cancers start in the transformation zone.



Most cervical cancers begin in the cells lining the cervix. 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 section, "Can cervical cancer be prevented?").

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 start in the squamous cells that cover the surface of the exocervix. Under the microscope, this type of cancer is made up of cells that are like squamous cells.

Most of the remaining types of cervical cancers are adenocarcinomas. Cervical adenocarcinomas seem to have become more common in the last 20 to 30 years. Cervical adenocarcinoma develops from the mucus-producing gland cells of the endocervix. 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, pre-cancerous cells will remain unchanged and 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 and specific types of treatment for pre-cancers are discussed in the section, "Can cervical cancer be prevented?"

Importance of cervical cancer screening

The goal of screening for cervical cancer is to find cervix cell changes and early cervical cancers before they cause symptoms. *Screening* refers to the use of tests and exams to find a disease, such as cancer, in people who do not have any symptoms. *Early detection* means applying a strategy that results in an earlier diagnosis of cervical cancer than otherwise might have occurred. Screening tests offer the best chance to detect cervical cancer 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.

Cancer of the cervix may be prevented or detected early by regular screening with the Pap test (sometimes combined with a test for human papilloma virus). If it is detected early, cervical cancer is one of the most successfully treatable cancers. In the United States, the cervical cancer death rate declined by almost 70% between 1955 and 1992, in large part due to the effectiveness of Pap test screening. The death rate from cervical cancer continued to decline until 2003. Since then it has remained stable in white women, but has gone down in African-American women.

Despite the recognized benefits of cervical cancer screening, not all American women take advantage of it. About half of the cervical cancers diagnosed in the United States are found in women who were never screened for the disease, with another 10% found in women who hadn't been screened within the past 5 years. In particular, older women, those without health insurance, and women who are recent immigrants are less likely to have regular 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, rather than as pre-cancers or early cancers.

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. When a woman develops cervical cancer or pre-cancerous changes of the cervix, it is not possible to say with certainty that a particular risk factor was the cause.

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 is 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 100 related viruses, some of which cause a type of growth called a *papilloma*, or more commonly known as *warts*. HPV can infect cells on the surface of the skin, genitals, anus, mouth and throat, but not the blood or most internal organs such as the heart or lungs. Doctors believe that women must have been infected by HPV before they will develop cervical cancer.

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. Still other 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. They are called *low-risk* types of HPV because they are seldom linked to cervical cancer.

Certain 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. In fact, doctors believe that a woman must be infected by HPV before she develops cervical cancer. The high-risk types include HPV 16, HPV 18, HPV 31, HPV 33, and HPV 45, as well as some others. 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 may 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 may 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 "Things to do to prevent pre-cancers" section in this document or ask for our document *Human Papilloma Virus (HPV), Cancer, and HPV Vaccines: Frequently Asked Questions*.

Although scientists believe that it is 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, contributing 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 body's immune system and places women at higher risk for HPV infection. This may explain the increased risk of cervical cancer in women with AIDS. Also, scientists believe that the immune system is important in destroying cancer cells and slowing their growth and spread. In women infected with 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 women 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 is 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). Infection with chlamydia often causes no symptoms in women. A woman may not know that she is infected at all unless she is tested for chlamydia when she gets her pelvic exam.

Diet

Women with diets low in fruits and vegetables may be at increased risk for cervical cancer. Also, overweight women are more likely to develop adenocarcinoma of the cervix.

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 recent 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 may 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.

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 the immune system of pregnant women might be weaker, allowing for HPV infection and cancer growth.

Young age at the 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 may 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 is 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 pre-cancers 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.

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 this familial tendency is caused by an inherited condition that makes some women less able to fight off HPV infection than others.

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 is cancer, ignoring symptoms may 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.

Things to do to prevent pre-cancers

Avoid being exposed to 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 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
- Having many sexual partners
- Having a partner who has had many sex partners

- Having sex with uncircumcised males

Waiting to have sex until you are older can help you avoid HPV. It also helps to limit your number of sexual partners and to avoid having sex with someone who has had many other sexual partners. Although the virus most often spreads between a man and a woman, HPV infection and cervical cancer 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 is required 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 and men

For men, the 2 main factors influencing the risk of genital HPV infection are circumcision and the number of sexual 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).

Condoms and HPV

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 diseases. Condoms (when used by the male partner) also seem to help the HPV infection and cervical pre-cancers go away faster.

Don't smoke

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

Get vaccinated

Vaccines have been developed that can protect women from HPV infections. So far, a vaccine that protects against HPV types 6, 11, 16 and 18 (Gardasil[®]) and one that protects against types 16 and 18 (Cervarix[®]) have been studied and approved for use in this country by the FDA. Both 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.

In clinical trials, both vaccines prevented pre-cancers and cancers of the cervix caused by HPV types 16 and 18. Gardasil also prevented anal, vaginal, and vulvar cancers caused by those HPV types, as well as genital warts caused by HPV types 6 and 11. Cervarix also provides some protection against infection and pre-cancers of the cervix caused by high-risk HPV types other than HPV 16 and 18. It has also been shown to prevent anal infection with HPV types 16 and 18.

Both 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 vaccine should be given before a person starts having sex.

In 2009, the Federal Advisory Committee on Immunization Practices (ACIP) published updated recommendations for HPV vaccination in girls and young women. It recommended that females aged 11 to 12 routinely be vaccinated 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. Either of the 2 vaccines, Cervarix or Gardasil, may be used to prevent cervical cancers and pre-cancers. However, the ACIP recommends using Gardasil to prevent genital warts as well as cervical cancers and pre-cancers.

The American Cancer Society guidelines also recommend 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. These vaccines have been tested in older women, and do seem to be effective in producing an immune reaction to the HPV types in the vaccine and also reduce cervical cancers and pre-cancers in those vaccinated. Studies in males have shown that Gardasil can prevent anal cancers and pre-cancers as well as anal and genital warts in men, and it has also been approved for that use. As new information on Cervarix, Gardasil, and other new products becomes available, these guidelines will be updated.

These vaccines are expensive -- costing about \$375 for the vaccine series (not including any doctor's fee or the cost of giving the injections). Either vaccine should be covered by

most medical insurance plans (if given according to ACIP guidelines). It should also be covered by government programs that pay for vaccinations in children under 18. But because vaccination costs so much, you might want to check your coverage with your insurance company before getting the vaccine.

It is important to realize that neither 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, *Human Papilloma Virus (HPV), Cancer, and HPV Vaccines: Frequently Asked Questions*.

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 the tests 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 Pap tests, even after they've been vaccinated. Most invasive cervical cancers are found in women who have not had regular Pap tests.

The American Cancer Society recommends the following guidelines for early detection:

- 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 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 is discussed later in this section 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 correct. 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 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. These women should have follow-up testing as recommended by their healthcare team.

The Papanicolaou (Pap) test

The Pap test is the main screening test for cervical cancer and pre-cancerous changes.

Although the Pap test has been more successful than any other screening test in preventing a cancer, it is not perfect. One of the limitations of the Pap test is that it needs 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 is not a good idea to have this test less often than American Cancer Society guidelines recommend.

Pelvic exam versus 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 at the start of the 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 tests is needed to find early cervical cancer or pre-cancers.

How the Pap test is done

Cytology is the branch of science that deals with the structure and function of cells. It also refers to tests to diagnose cancer and pre-cancer by looking at cells under the microscope. The Pap test is a procedure used to collect cells from the cervix for cervical cytology testing.

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 (see illustration in “What is cervical cancer?” section). 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). The cell samples are then prepared so that they can be examined under a microscope in the laboratory. This is done in 2 main ways.

Conventional cytology: One way is to smear the sample directly onto a glass microscope slide, which is then sent to the laboratory. For about 50 years, all cervical cytology samples were handled this way. This method works quite well and is relatively inexpensive, but it does have some drawbacks. One problem with this method is that the cells smeared onto the slide are sometimes piled up on each other, making it hard to see the cells at the bottom of the pile. Also, white blood cells (pus), increased mucus, yeast cells, or bacteria from infection or inflammation can hide the cervical cells. Another problem with direct smears is that if the slides are not treated with a preservative right away, the cells can dry out. This can make it difficult to tell if there is something wrong with the cells. If the cervical cells cannot be seen well (because of any of these problems), the test is less accurate, and it may need to be done again.

Liquid-based cytology: The other way is to put the sample of cells from the cervix into a special preservative liquid (instead of putting them on a slide directly). This is sent to the lab. Technicians then use special lab instruments to spread some of the cells in the liquid onto glass slides to look at under the microscope. This method is called *liquid-based cytology*, or a *liquid-based Pap test*. The liquid helps remove some of the mucus, bacteria, yeast, and pus cells in a sample. It also allows the cervical cells to be spread more evenly on the slide and keeps them from drying out and becoming distorted. Cells kept in the liquid can also be tested for HPV. Using liquid-based testing may reduce the chance that the Pap test will need to be repeated, but it does not seem to find more pre-cancers than a regular Pap test. The liquid-based test is also 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 more expensive than a usual Pap test.

Another way to improve the Pap test is by using computerized instruments that can spot abnormal cells in Pap tests. A machine that can read Pap tests has been approved by the FDA to read Pap tests first (instead of them being examined by a technologist). It is also approved by the FDA for rechecking Pap test results that were read as normal by technologists. Any smear identified as abnormal by the machine would then be reviewed by a doctor or a technologist.

Computerized instruments can find abnormal cells that technologists sometimes miss. Most of the abnormal cells found this way are in rather early stages, such as atypical

squamous cells (ASCs), but sometimes high-grade abnormalities missed by human testing can be found. Scientists do not know yet whether the instrument can find enough high-grade abnormalities missed by human testing to have a real impact on preventing invasive cervical cancers. Automated testing also increases the cost of cervical cytology testing.

For now, the best way to detect cervical cancer early is to make certain that all women are tested according to American Cancer Society guidelines. 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, jellies or other vaginal creams 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.

Is there a Pap test you can do at home?

Doctors have been trying to find ways to get more women involved in cervical cancer screening. Some have proposed methods that would allow women to take cervical cell samples at home. For this test, a woman would collect cervical cells herself by inserting a small plastic applicator into the vagina and moving it around on the cervix. This would be placed in a special container to preserve the cells. Women in poorer countries have used this method to check for sexually transmitted diseases, and it has also been useful to check for HPV infections. So far, however, no "home-based" Pap test has been approved for use in the United States. Currently, the American Cancer Society does not recommend any "at-home" Pap test.

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, and
- 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: The second category, epithelial cell abnormalities, means that the cells lining the cervix or vagina show changes that might be cancer or a pre-cancerous condition. This category is divided into several groups for squamous cells and glandular cells. The epithelial cell abnormalities for squamous cells are:

Atypical squamous cells (ASCs): This term is 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 is a pre-cancer. This group is further divided into 2 groups, 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). Most of the time, cells labeled ASC-US are not pre-cancer. Some doctors will recommend repeating the Pap test in 6 months. Some doctors use the HPV DNA test to help them decide whether or not to do a colposcopy. If a high-risk type of HPV is found, the doctor is more likely to order a colposcopy. (Colposcopy is discussed in more detail in the section, "Other tests for women with abnormal cervical cytology results.")

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

Squamous intraepithelial lesions (SILs): These abnormalities are subdivided into low-grade SIL and high-grade SIL. In low-grade SIL, the cells are mildly abnormal, while in high-grade SIL, the cells are severely abnormal. High-grade SILs are less likely than low-grade SILs 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. A Pap test cannot tell for certain whether a woman has a high- or low-grade SIL. It merely fits the result into one of these abnormal categories. All patients over the age of 20 with a Pap test result of SIL should have colposcopy. The need for treatment is based on the results of the biopsies done at colposcopy. Since most SILs are positive for HPV, HPV testing is not used to decide if a woman with SIL results on a Pap test needs a colposcopy.

Pap testing is not recommended for women 20 years old or younger, but if they do have a Pap test that shows low-grade SIL, they should have a repeat Pap test in a year. If they have a high-grade SIL, colposcopy is recommended.

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.

The Bethesda System also describes epithelial cell abnormalities for glandular cells.

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.

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 can be used in 2 situations:

- The HPV gene test can be used in combination with the Pap test to screen for cervical cancer in women 30 years of age and older (see American Cancer Society screening guidelines). It does not replace the Pap test. 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 this reason, the HPV DNA test is not recommended as a screening test in women under 30. For more information, see the American Cancer Society documents, *What Women Should Know About Cervix Cancer and the Human Papilloma Virus* and *Thinking About Testing for HPV?*
- 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 next section).

Other tests for women with abnormal cervical cytology 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. These tests are commonly used when the results of a Pap test are reported as SIL, atypical glandular cells, or cancer. If a biopsy shows a pre-cancer, doctors will take steps to keep an actual cancer from developing.

Doctors are less certain about what to do when the Pap test result shows atypical squamous cells (ASC). In deciding what to do, some doctors take into account your age, your previous Pap test results, whether you have any cervical cancer risk factors, whether you have remembered to have Pap tests done in the past, and whether the test result is ASC-H or ASC-US. For women at least 21 years of age with ASC-US, experts recommend either a colposcopy, a repeat Pap test in 6 months, or HPV DNA testing. If the woman is HPV-positive, colposcopy will be done. For ASC-H, many doctors will recommend colposcopy and biopsy.

Pap testing is not recommended for women 20 years old or younger, but if they do have Pap test results that show ASC-US, they are likely to be observed but not treated.

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 with 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 is not painful, has no side effects, and can be done safely even if you are pregnant. Like the Pap test, it is 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 is 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.

How women with abnormal Pap test results are treated to prevent cervical cancers 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). Other options include a cold knife cone biopsy and destroying the abnormal cells with cryosurgery or laser surgery.

During cryosurgery, the doctor uses a metal probe cooled with liquid nitrogen to kill the abnormal cells by freezing them.

In laser surgery, the doctor uses a focused beam of high-energy light to vaporize (burn off) the abnormal tissue. This is done through the vagina, with local anesthesia.

Both cryosurgery and laser surgery 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.

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.

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 ACS 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. Most of those plans are covered by state laws, which vary by state.

State efforts to ensure coverage of cervical cancer screening for private health insurance

Twenty-six states and the District of Columbia now require private health insurers to cover annual cervical cancer screening services (see table).

A few states have also enacted laws specifically requiring managed care organizations such as health maintenance organizations (HMOs) and preferred provider organizations (PPOs) to cover cervical cancer screening.

Some states have ensured that public employee health benefit plans cover cervical cancer screening. Although Maryland does not have a statewide benefit for cervical cancer screening, they do have a unique law requiring hospitals to offer a Pap test to adult female inpatients. Nebraska has a law that requires the Department of Health to contract with health clinics of American Indian tribes to cover cervical cancer detection services. Individual state laws vary widely. Ask your health care provider what coverage is mandatory in your state

States With Laws Assuring Coverage of Cervical Cancer Screening (March 2011)

State	Private Insurance	Other
Alaska	Annual Pap test for persons age 18 and over	Co-pay, deductibles, and/or co-insurance may apply
California	Annual Pap test, pelvic exam, and HPV testing Need referral of patient's health care provider	Co-pay, deductibles, and/or co-insurance may apply
Colorado	Does not specify	Co-pay, deductibles, and/or co-insurance may apply
Delaware	Annual Pap test for persons age 18 and over	Co-pay, deductibles, and/or co-insurance may apply
District of Columbia	Annual Pap test More frequent tests if recommended by a physician	
Georgia	Annual Pap test Need referral of patient's health care provider More frequent tests if recommended by a physician	Co-pay, deductibles, and/or co-insurance may apply
Illinois	Annual Pap test	
Kansas	Annual Pap test Need referral of patient's health care provider	Co-pay, deductibles, and/or co-insurance may apply
Louisiana	Annual Pap test	
Maine	Annual Pap test and pelvic exam	

	Need referral of patient's health care provider	
Maryland	Covers HPV testing only, according to ACOG Guidelines (see below)	Co-pay, deductibles, and/or co-insurance may apply
Massachusetts	Annual Pap test for persons age 18 and over	
Minnesota	Cover Pap test when ordered by doctor according to standard practice	
Missouri	Cover Pap test and pelvic exam according to ACS guidelines (see below)	Co-pay, deductibles, and/or co-insurance may apply
Nevada	Annual Pap test for persons age 18 and over	
New Jersey	Cover Pap test every 2 years for persons 20 and over More frequent testing if recommended by a doctor Need referral of patient's health care provider	Certain specified HMOs must only offer and not provide coverage
New Mexico	Cover Pap test, pelvic exam, and HPV testing for persons age 18 and over Medical standards determine how often testing should be done Need referral of patient's health care provider	Co-pay, deductibles, and/or co-insurance may apply
New York	Annual Pap test and pelvic exam for persons age 18 and over	Co-pay, deductibles, and/or co-insurance may apply
North Carolina	Cover Pap test and HPV testing according to ACS guidelines (see below) or those established by the NC Advisory Committee on Cancer Coordination and Control	Co-pay, deductibles, and/or co-insurance may apply
Ohio	Cover Pap test	
Oregon	Annual Pap test and pelvic exam for persons age 18-64 More frequent testing if recommended by a doctor	
Pennsylvania	Cover Pap test and pelvic exam according to ACOG Guidelines (see below)	
Rhode Island	Cover Pap test according to ACS Guidelines (see below)	
South Carolina	Annual Pap test More frequent testing if recommended by a doctor	Co-pay, deductibles, and/or co-insurance may apply

	Need referral of patient's health care provider	
Texas	Annual Pap test and HPV test when done at the same time, for persons age 18 and over, according to ACOG (or similar national organization) Guidelines (see below)	
Virginia	Annual Pap test	
West Virginia	Annual Pap test and HPV testing for persons age 18 and over, according to ACOG Guidelines or USPSTF Recommendations (see below)	Co-pay, deductibles, and/or co-insurance may apply
Wyoming	Cover Pap test and pelvic exam	Co-insurance may apply

American College of Obstetricians and Gynecologists (ACOG) Guidelines: Cervical cancer screening should begin at 21. Guidelines for subsequent screening differ based on age, type of screening test, and prior test results.

American Cancer Society (ACS) Guidelines: Cervical cancer screening should begin at 21 years of age. Guidelines for subsequent screening differ based on age, type of screening test, and prior test results.

United States Preventive Services Task Force (USPSTF) Recommendations: The USPSTF strongly recommends screening for cervical cancer in women who have been sexually active and have a cervix beginning at age 21.

Source: National Cancer Institute: State Cancer Legislative Database Program, Bethesda, MD. 2011.

Self-insured plans

ERISA, or self-insured plans, are not regulated at the state level, and so do not have to follow state laws about cervical cancer screening. They are covered by the ACA and so most are required to cover cervical cancer screening. The exception is any self-insured plan that was in place prior to the ACA. These plans are called *grandfathered*, and they don't have to provide coverage based on what the ACA says.

Self-insured plans are typically large employers. 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 copay, 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.

Since 1991, the program has provided millions of screening exams to underserved women, diagnosed more than 52,000 breast cancers, more than 130,000 pre-cancerous cervical lesions, and more than 2,800 cervical cancers. These accomplishments demonstrate a truly nationwide effort. However, due to limited resources, only about 15% of all eligible women are served nationwide.

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.

HPV vaccine costs

It is 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 do not 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 available in Spanish)

Human Papilloma Virus (HPV), Cancer, and HPV Vaccines: Frequently Asked Questions (also available in Spanish)

Thinking About Testing for HPV? (also available in Spanish)

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

National organizations and Web sites*

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

Web site: 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)

Web site: www.cdc.gov/cancer/nbccedp

National Cervical Cancer Coalition

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

Web site: www.nccc-online.org

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

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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