



CERVICAL CANCER

What is cancer?

The body is made up of hundreds of millions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of out-of-control growth of abnormal cells.

Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. Cancer cells can also invade (grow into) other tissues, something that normal cells cannot do. Growing out of control and invading other tissues are what makes a cell a cancer cell.

Cells become cancer cells because of damage to DNA. DNA is in every cell and directs all its actions. In a normal cell, when DNA gets damaged the cell either repairs the damage or the cell dies. In cancer cells, the damaged DNA is not repaired, but the cell doesn't die like it should. Instead, this cell goes on making new cells that the body does not need. These new cells will all have the same damaged DNA as the first cell does.

People can inherit damaged DNA, but most DNA damage is caused by mistakes that happen while the normal cell is reproducing or by something in our environment. Sometimes the cause of the DNA damage is something obvious, like cigarette smoking. But often no clear cause is found.

In most cases the cancer cells form a tumor. Some cancers, like leukemia, rarely form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

Cancer cells often travel to other parts of the body, where they begin to grow and form new tumors that replace normal tissue. This process is called metastasis. It happens when the cancer cells get into the bloodstream or lymph vessels of our body.

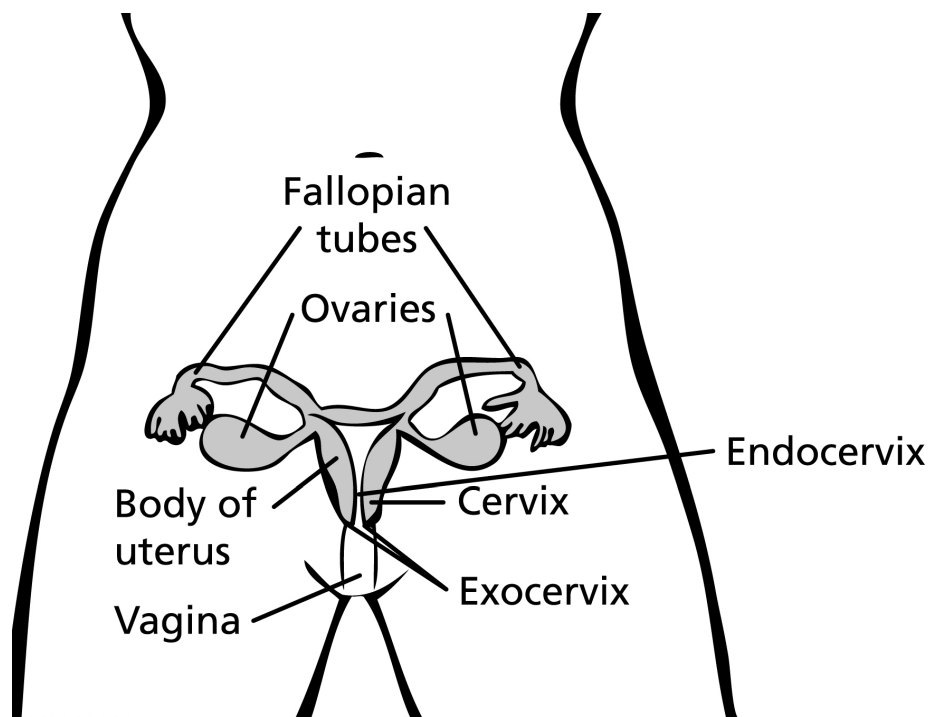
No matter where a cancer may spread, it is always named for the place where it started. For example, breast cancer that has spread to the liver is still called breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bone is metastatic prostate cancer, not bone cancer.

Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer.

Not all tumors are cancerous. Tumors that aren't cancer are called benign. Benign tumors can cause problems – they can grow very large and press on healthy organs and tissues. But they cannot grow into (invade) other tissues. Because they can't invade, they also can't spread to other parts of the body (metastasize). These tumors are almost never life threatening.

What is cervical cancer?

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 baby 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 ectocervix) and *glandular* cells (on the endocervix). The place where 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 first 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 the development of cancer (see "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 cancers: *squamous cell carcinoma* and *adenocarcinoma*. About 80% to 90% of cervical cancers are squamous cell carcinomas. These cancers are from 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. Squamous cell carcinomas most often begin where the exocervix joins the endocervix.

Most of the remaining cervical cancers are adenocarcinomas. Adenocarcinomas are becoming more common in women born 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 of the women with pre-cancers of the cervix will develop cancer. The change from cervical pre-cancer to cervical cancer usually takes several years -- but it can happen in less than a year. For most women, pre-cancerous cells will 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?"

Pre-cancerous changes are separated into different categories based on how the cells of the cervix look under a microscope. These categories are discussed in the section, "Can cervical cancer be prevented?"

Although almost all cervical cancers are either squamous cell carcinomas or adenocarcinomas, other types of cancer also can develop in the cervix. These other types, such as melanoma, sarcoma, and lymphoma, occur more commonly in other parts of the body.

This document discusses the more common cervical cancer types, and will not further discuss these rare types.

What are the key statistics about cervical cancer?

The American Cancer Society's most recent estimates for cervical cancer in the United States are for 2009:

- about 11,270 new cases of invasive cervical cancer will be diagnosed.
- about 4,070 women will die from cervical cancer.

Some researchers estimate that non-invasive cervical cancer (carcinoma in situ) is about 4 times more common than invasive cervical cancer.

Cervical cancer was once one of the most common causes of cancer death for American women. Then, between 1955 and 1992, the cervical cancer death rate declined by almost 70%. The main reason for this change was the increased use of the Pap test. This screening procedure can find changes in the cervix before cancer develops. It can also find cervical cancer early -- in its most curable stage. The death rate from cervical cancer continues to decline by nearly 4% each year.

Cervical cancer tends to occur in midlife. Most cases are found in women younger than 50. It rarely develops in women younger than 20. Many older women do not realize that the risk of developing cervical cancer is still present as they age. Almost 20% of women with cervical cancer are diagnosed when they are over 65. That is why it is important for older women to continue having regular Pap tests. See the section, "Can cervical cancer be prevented?" for more specific information on current American Cancer Society screening recommendations.

In the United States, cervical cancer occurs most often in Hispanic women; at a rate that is more than twice what is seen in non-Hispanic white women. African-American women develop this cancer about 50% more often than non-Hispanic white women.

The 5-year relative survival rate for the earliest stage of invasive cervical cancer is 92%. The overall (all stages combined) 5-year survival rate for cervical cancer is about 71%.

The *5-year survival rate* refers to the percentage of patients who live at least 5 years after their cancer is diagnosed. Five-year rates are used to produce a standard way of discussing prognosis. Of course, many people live much longer than 5 years. Five-year relative survival rates assume that some people will die of other causes and compare the observed survival with that expected for people without the cancer. This is a more accurate way to describe the prognosis for patients with a particular type and stage of cancer. Five-year rates are used to produce a standard way to discuss prognosis, or outlook for survival.

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 developing cervical cancer. Women without any of these risk factors rarely develop cervical cancer. Although these risk factors increase the odds of developing cervical cancer, many women with these risks do not develop this disease. When a woman develops cervical cancer or pre-cancerous changes, it may not be possible to say with certainty that a particular risk factor was the cause.

In thinking about risk factors, it helps to focus on those you can change or avoid (like smoking or human papilloma virus infection), rather than those you cannot (such as your age and family history). However, it is still important 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 that can infect cells on the surface of the skin, genitals, anus, mouth and throat. They are called papilloma viruses because some of them cause a type of growth called a papilloma. Papillomas are not cancers, and are more commonly called warts. HPV is passed from one person to another during skin-to-skin

contact. HPV can be spread during sex - including vaginal intercourse, anal intercourse, and even during oral sex. Still, intercourse doesn't have to take place for HPV to spread from one person to another. All that is needed is for there to be skin-to-skin contact with an area of the body infected with HPV.

Doctors believe that women must be infected by HPV before they develop cervical cancer. Certain types of HPV are called *high-risk types* because they are often the cause of cancer of the cervix. These 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. The high-risk types are also associated with other anogenital cancers such as vulvar and vaginal cancer in women, penile cancer in men, and anal cancer in both men and women.

Different types of HPVs 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. HPV only infects cells on the surface of the body, including those of the anus and genitals, but cannot infect the blood or most internal organs such as the heart or lungs.

Still other types of HPV may cause warts on or around the female and male 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. Since these 2 types are seldom linked to cervical cancer, they are called *low-risk types* of HPV.

Many women become infected with HPV, but very few will ever develop cervical cancer. In most cases the body's immune system fights off the virus, and the infection goes away without any treatment. For reasons that we don't understand, in some women the infection persists and can go on to cause cervical cancer. Although there is currently no cure for HPV infection, there are ways to treat the warts and abnormal cell growth that HPV causes.

The Pap test looks for changes in cervical cells caused by HPV infection. Newer tests look for the infections themselves by finding genes (DNA) from HPV in the cells. Some doctors use the test for HPV 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.

HPV infections occur mainly in young women and are less common in women older than 30. The reason for this is not clear. Uncircumcised men are thought to be more likely to have the virus and be able to pass it on to someone else. HPV infection can be present for years without any symptoms. Even when someone doesn't have visible warts (or any other symptom), he or she can still be infected with HPV and pass the virus to somebody else.

Condoms ("rubbers") do provide some protection against HPV, but they cannot completely protect against infection. This is because HPV can still be passed from one person to another by skin-to-skin contact with an HPV-infected area of the body that is not covered by a condom - like the skin in the genital or anal area. Still, condoms can help the body get rid of

an HPV infection faster, so that abnormal pap tests become normal again in less time. Also, it is important to use condoms to protect against AIDS and other sexually transmitted illnesses that are passed on through some body fluids.

Vaccines have been developed to help prevent infection with some types of HPV. Right now, 2 different HPV vaccines have been approved for use in the United States by the Food and Drug Administration (FDA). One vaccine is called Gardasil®, and it protects against HPV types 6, 11, 16, and 18. Another HPV vaccine, known as Cervarix®, protects against HPV types 16 and 18. Both of these vaccines have been shown to reduce the risk of cervical cancer. More HPV vaccines are being developed and tested.

Although it is necessary to have 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 the 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.

Immunosuppression

Human immunodeficiency virus (HIV), the virus that causes AIDS, damages the body's immune system and places women at higher risk for HPV infections. This may explain the increased risk of cervical cancer for women with AIDS. Scientists believe that the immune system is important in destroying cancer cells and slowing their growth and spread. In women with HIV, a cervical pre-cancer might develop into an invasive cancer faster than it normally would.

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 evidence of past or current chlamydia infection (compared with women who have 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 a recent 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 the potential risks. 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 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) develop clear-cell adenocarcinoma of the vagina or cervix more often than would normally be expected. This type of cancer is extremely rare in non-DES exposed women. There is about 1 case of this

type of cancer in every 1,000 women whose mothers took DES during 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.

Family history of cervical cancer

Cervical cancer may run in some families. If your mother or sister had cervical cancer, your chances of developing the disease are 2 to 3 times higher than if no one in the family had it. Some researchers suspect that 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 may be more likely to have one or more of the other non-genetic risk factors previously described in this section.]

Do we know what causes cervical cancer?

In recent years, scientists have made much progress toward understanding what happens in cells of the cervix when cancer develops. In addition, they have identified several risk factors that increase the odds that a woman might develop cervical cancer (see the previous section).

The development of normal human cells mostly depends on the information contained in the cells' chromosomes. Chromosomes are large molecules of DNA. DNA is the chemical that carries the instructions for nearly everything our cells do. We usually look like our parents because they are the source of our DNA. However, DNA affects more than the way we look.

Some genes (packets of our DNA) have instructions for controlling when our cells grow and divide. Certain genes that promote cell division are called *oncogenes*. Others that slow down cell division or cause cells to die at the right time are called *tumor suppressor genes*. Cancers can be caused by DNA mutations (gene defects) that turn on oncogenes or turn off tumor suppressor genes. HPV causes the production of 2 proteins known as E6 and E7. When these proteins are produced, they turn off some tumor suppressor genes. This may allow the cervical lining cells to grow uncontrollably, which in some cases will lead to cancer.

But HPV does not completely explain what causes cervical cancer. Most women with HPV don't get cervical cancer, and certain other risk factors, like smoking and HIV infection, influence which women exposed to HPV are more likely to develop cervical cancer.

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. The first way is to find and treat pre-cancers before they become cancerous, and the second is to prevent the pre-cancers.

Finding and treating pre-cancerous changes

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 (or Pap smear) is the most common way to do this. If a pre-cancer is found it can be treated, stopping cervical cancer before it really starts. 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) 3 years after they start having sex (vaginal intercourse). A woman who waits until she is over 18 to have sex should start screening no later than age 21. A conventional (regular Pap) test should be done every year. If a liquid-based Pap test is used instead, testing should be done every 2 years.
- Beginning at age 30, many women who have had 3 normal Pap test results in a row may be tested less often, every 2 to 3 years. Either the conventional (regular) Pap test or the liquid-based Pap test can be used. Some women should continue getting tested yearly -- such as women exposed to DES before birth, those with a history of treatment for a pre-cancer, and those with a weakened immune system (such as from HIV infection, organ transplant, chemotherapy, or chronic steroid use).
- Another reasonable option for women over 30 (who have normal immune systems and no abnormal Pap results) is to get tested only every 3 years with a Pap test plus the HPV DNA test (see below for more information on this test). The Pap test used can be either the regular or the liquid-based Pap test.
- Women 70 years of age or older who have had 3 or more normal Pap tests in a row and no abnormal Pap test results in the last 10 years may choose to stop having cervical cancer testing. Women with a history of cervical cancer, DES exposure

before birth, HIV infection, or a weakened immune system should continue to have testing as long as they are in good health.

- Women who have had a total hysterectomy (removal of the uterus and cervix) may also choose to stop having cervical cancer testing, unless the surgery was done as a treatment for cervical cancer or pre-cancer. Women who have had a hysterectomy without removal of the cervix (a supra-cervical hysterectomy) need to continue cervical cancer screening. They should continue to follow the guidelines above.

Some women believe that they can stop having Pap tests once they have stopped having children. This is not correct. They should continue to follow American Cancer Society guidelines.

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 examined in the best laboratories), it is not a good idea to have this test less often than American Cancer Society guidelines recommend.

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.
- Do not douche for 48 hours before the test.
- Do not have sexual intercourse for 48 hours before the test.
- Do not douche or use tampons, birth control foams, jellies, or other vaginal creams or vaginal medicines for 48 hours before the test.

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 cervical cancer at an early stage or abnormal cells of the cervix. 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 must remove 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 only Pap tests give information on 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 by looking at cells under the microscope. The Pap test (or Pap smear) 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 (the surface of the cervix that is closest to the vagina). A small brush or a cotton-tipped swab is then inserted into the cervical opening to take a sample from the endocervix (the inside part of the cervix that is closest to the body of the uterus). There are 2 main ways to prepare the cell samples so that they can be examined under a microscope in the laboratory.

Conventional cytology

One method is to smear the sample directly onto a glass microscope slide, which is then sent to the laboratory. All cervical cytology samples were handled in this way for at least 50 years. 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 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 Pap smear may need to be repeated.

Liquid-based cytology

Another method 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 reduces the chance that the Pap test will need to be repeated, but it does not 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 also more expensive than the usual Pap test.

Another way to improve the Pap test is by using computerized instruments to spot the abnormal cells on the slides. An instrument to do this 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 this instrument 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 in this way are in rather early stages, such as atypical squamous cells 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 the 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.

How Pap test results are reported

The most widely used system for describing Pap test results is The Bethesda System (TBS). This system has been revised twice since it was developed in 1988: first in 1991 and, most recently, in 2001. The information that follows is based on the 2001 version. The general categories are:

- 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 infections with yeast, herpes, or *Trichomonas vaginalis* (a microscopic parasite), for example. Some cases 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 of the lining layer of the cervix 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 called:

- *Atypical squamous cells (ASCs)*; these are further divided into ASC-US and ASC-H
- *Squamous intraepithelial lesions (SILs)*; these are separated into low-grade SILs and high-grade SILs
- *Squamous cell carcinoma*

Atypical squamous cells: This category includes atypical squamous cells of uncertain significance (ASC-US). 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 the cause is infection or irritation, or if it is a pre-cancer. Most of the time, cells labeled ASC-US are not pre-cancer. Some doctors will recommend repeating the Pap test after 6 months. Some doctors use the HPV DNA test to decide whether or not to do a colposcopy. If a high-risk type of HPV is detected, the doctor is 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 high grade SIL is suspected. Colposcopy is recommended.

Squamous intraepithelial lesions (SILs): These abnormalities are divided into low-grade SIL and high-grade SIL. High-grade SILs are less likely than low-grade SILs to go away without treatment. High-grade SILs are also more likely to eventually develop into cancer if they are not treated. Treatment can cure all SILs and prevent true cancer from developing. A Pap test cannot tell for certain if a woman has a high- or low-grade SIL. It merely fits the result into one of these abnormal categories. Any patient with an SIL should have colposcopy. The need for treatment is based on the results of the biopsies obtained during colposcopy. Since most SILs are positive for HPV, HPV testing is not used to determine the need for colposcopy in a woman with SIL on a Pap.

Squamous cell carcinoma: This result means that the woman is likely to have an invasive squamous cell 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 reported as adenocarcinomas. In some cases, the pathologist examining the cells can suggest 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, they are called *atypical glandular cells*. The patient usually will have more testing if her cervical cytology result shows atypical glandular cells.

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 that are most likely to cause cervical cancer (high-risk types) 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 in some cases can even be done on the same sample. The HPV DNA test is used in 2 different situations.

- The FDA has approved the HPV DNA test to be used in combination with the Pap test to screen for cervical cancer in women over 30 years old (see American Cancer Society screening guidelines above). 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 document, *What Every Woman Should Know About Cervical Cancer and the Human Papilloma Virus*.
- The HPV DNA test can also be used for women of any age who have slightly abnormal Pap test results (ASC-US) to find out if they might need more testing or treatment (see next section).

Other tests for women with abnormal cervical cytology results

The Pap test is a screening test, not a diagnostic test. 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 used for a Pap test result of SIL or atypical glandular cells. 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, 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. Women 20 years old or younger with Pap test results that show ASC-US are likely to be observed without treatment. 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.

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 stays outside the body) that has magnifying lenses (like binoculars). 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 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 whether an abnormal area is a pre-cancer, a true cancer, or neither.

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.

Colposcopic biopsy: For this type of biopsy, first the cervix is examined with a colposcope to find the abnormal areas. Using a biopsy forceps, a small (about 1/8-inch) section of the abnormal area on the surface of the cervix is removed. The biopsy procedure may cause mild cramping, brief pain, and some slight bleeding 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 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 that is lining the endocervical canal. This tissue sample is sent to the laboratory for examination. After this procedure, patients may feel a cramping pain, and they may also have some light bleeding.

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 start. The cone biopsy can also 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 a large amount of tissue has been removed, 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 [LLETZ]) and the cold knife cone biopsy.

- **Loop electrosurgical procedure (LEEP, LLETZ):** In 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 takes only about 10 minutes. You may have mild cramping during and after the procedure, and mild-to-moderate bleeding may persist 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 last for a few weeks.

How biopsy results are reported

The terms for reporting biopsy results are slightly different from The Bethesda System for reporting Pap test results. Pre-cancerous changes are called cervical intraepithelial neoplasia (CIN) or, rarely, dysplasia, instead of squamous intraepithelial lesion (SIL). The terms for reporting cancers (squamous cell carcinoma and adenocarcinoma) are the same.

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 can remove it with a loop electrosurgical procedure (LEEP or LLETZ) or a cold knife cone biopsy. Other options include 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.

Things to do to prevent pre-cancers

Avoid being exposed to HPV

You can prevent most pre-cancers of the cervix by avoiding exposure to HPV. 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

Delay sex

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. Remember, HPV does not always cause warts or any other symptoms; even someone infected with HPV for years may have no symptoms. Someone can have the virus and pass it on without knowing it.

Use condoms

Condoms provide some protection against HPV. One study found that when condoms are used correctly they can lower the HPV infection rate by about 70% if they are used every time sex occurs. Condoms cannot protect completely 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. Cervarix was recently approved (in 2009) for use in the United States by the FDA, while Gardasil has been approved for use in this country since 2006. In October 2009, the FDA also approved the use of Gardasil in males to prevent genital warts. Both vaccines require a series of 3 injections over a 6-month period. The 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. Cervarix is approved for use in girls and young women ages 10 to 25 years, while Gardasil is approved for those 9 to 26 years old.

In clinical trials, both vaccines prevented cervical cancers and pre-cancers caused by HPV types 16 and 18. Gardasil also prevented genital warts caused by HPV types 6 and 11. Both Gardasil and Cervarix 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 recommendations for HPV vaccination. It recommended that females aged 11 to 12 routinely receive HPV vaccination with the full series of 3 shots. Females as young as age 9 may also receive the 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,. The ACIP recommends using Gardasil to prevent cervical cancers, cervical cancers, and genital warts,.

These vaccines should be given with caution to anyone with severe allergies. Women with a severe allergy to latex should not take the Cervarix vaccine, and those with a severe allergy to yeast should not receive Gardasil.

The American Cancer Society guidelines recommend that the cervical cancer vaccine be routinely given to females aged 11 to 12 and as early as age 9 years 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 enough proof that catch-up vaccination for all woman 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 before making a decision about getting vaccinated. They should discuss the risks of previous HPV exposure and potential benefit from vaccination before deciding to get the vaccine. Research has shown that it is effective in producing an immune reaction to the HPV types in the vaccine and also reduces cervical cancers and pre-cancers in those women who get vaccinated. These vaccines have also been studied in older women and males. As new information on Cervarix, Gardasil, and other new products becomes available, these guidelines will be updated.

Both types of cervical cancer vaccines are expensive -- costing about \$375 for the full series of injections (not including the doctor's fee or the cost of giving the injections). It 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. Because this cost is so high, you may want to check your coverage with your insurance company before getting the vaccine.

It is important to realize that the vaccine doesn't protect against all cancer-causing types of HPV, so routine Pap tests are still necessary. One other benefit of the Gardasil vaccine is that it protects against the 2 viruses that cause 90% of genital warts.

For more information on the vaccine and HPV, please see our document, *Human Papilloma Virus: Questions and Answers*.

Can cervical cancer be found early?

Cervical cancer can usually be found early by having regular Pap tests. As Pap testing became routine in this country, during the past half century pre-invasive lesions (pre-cancers) of the cervix became far more common than invasive cancer. Being alert to any signs and symptoms of cervical cancer (see "How is cervical cancer diagnosed?") can also help avoid unnecessary delays in diagnosis. Early detection greatly improves the chances of successful treatment and prevents any early cervical cell changes from becoming cancerous.

The importance of the Pap test in finding cervical cancer and pre-cancerous changes

In countries where women cannot get routine Pap tests, death from cervical cancer is much more common. In fact, cervical cancer is the major cause of cancer deaths in women in many developing countries. These cases are usually diagnosed at a late (invasive) stage, rather than as pre-cancers or early cancers.

Not all American women take advantage of the benefits of Pap test screening. Between 60% and 80% of American women who are diagnosed with invasive cervical cancer have not had a Pap test in the past 5 years. In fact, many of these women have never had a Pap test. In particular, elderly, African-American, and/or low-income women and women who are recent immigrants are less likely to have regular Pap tests.

Financial assistance for low-income women

Tests for breast cancer and cervical cancer are now more available to medically underserved women through the National Breast and Cervical Cancer Early Detection Program (NBCCEDP). This program offers breast and cervical cancer early detection testing to women without health insurance for free or at very little cost.

The NBCCEDP tries to reach as many women in medically underserved communities as possible, including older women, women without health insurance, and women of racial and ethnic minority groups. Although each state runs its own program, the Centers for Disease Control and Prevention (CDC) give matching funds and support to each state program.

This program is offered mainly through nonprofit organizations and local health clinics, and is aimed at providing testing for breast and cervical cancer in medically underserved women. Each state's Department of Health will have information on how to contact the nearest participating program.

How is cervical cancer diagnosed?

Signs and symptoms of cervical cancer

Women with early cervical cancers and pre-cancers usually have no symptoms. Symptoms often do not begin until the cancer becomes invasive 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 (menstrual) periods that are longer or heavier 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 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 signs or other suspicious symptoms, you should see your health care professional right away. Ignoring symptoms may allow the cancer to progress to a more advanced stage and lower your chance for effective treatment.

Even better, don't wait for symptoms to appear. Have regular Pap tests and pelvic exams.

Your primary doctor can often treat pre-cancers. If there is a question of invasive cancer, your doctor will refer you to a gynecologic oncologist, a doctor who specializes in women's reproductive system cancers. Some patients will also be referred to a radiation oncologist, a doctor who specializes in treating cancers with radiation.

Diagnostic tests for cervical cancer

Many of the diagnostic tests described below are not necessary for every patient. Decisions about using these tests are based on the results of the physical exam and biopsy.

Medical history and physical exam

Getting your complete personal and family medical history is the first step your doctor will take in your consultation. This includes information related to risk factors and symptoms of cervical cancer. A complete physical exam will help evaluate your general state of health. In addition, special attention will be paid to your lymph nodes for evidence of metastasis (cancer spread).

Cystoscopy, proctoscopy, and examination under anesthesia

These are most often done in women who have large tumors. They are not necessary if the cancer is caught early.

In cystoscopy a slender tube with a lens and a light is placed into the bladder through the urethra. This lets the doctor check your bladder and urethra to see if cancer is growing into these areas. Biopsy samples can be removed during cystoscopy for pathologic (microscopic) testing. Cystoscopy can be done under a local anesthetic, but some patients may need general anesthesia. Your doctor will let you know what to expect before and after the procedure.

Proctoscopy is a visual inspection of the rectum through a lighted tube to check for spread of cervical cancer into your rectum.

Your doctor may also do a pelvic exam while you are under anesthesia to find out whether the cancer has spread beyond the cervix.

Imaging studies

If your doctor finds that you have cervical cancer, certain imaging studies may be done. These include magnetic resonance imaging (MRI) and computed tomography (CT) scans. These studies can show whether the cancer has spread beyond the cervix.

Chest x-ray: A plain x-ray of your chest will be done to see if your cancer has spread to your lungs. This is very unlikely unless your cancer is far advanced. This x-ray can be done in an outpatient setting. If the results are normal, you probably don't have cancer in your lungs.

Computed tomography (CT): The CT scan is an x-ray procedure that produces detailed cross-sectional images of your body. Instead of taking one picture, like a conventional x-ray, a CT scanner takes many pictures as it rotates around you. A computer then combines these pictures into an image of a slice of your body (think of a loaf of sliced bread). The machine takes pictures of multiple slices of the part of your body that is being studied. CT scans can help tell if your cancer has spread to the lymph nodes in the abdomen and pelvis. They are also used to see if the cancer has spread to the liver, lungs, or elsewhere in the body.

Before the first set of pictures is taken you may be asked to drink 1 to 2 pints of a contrast liquid. You may also receive an IV (intravenous) line through which a different kind of contrast is injected. This helps better outline structures in your body.

The IV contrast can cause your body to feel flushed (a feeling of warmth with some redness of the skin). A few people are allergic to the dye and can get hives. Rarely, more serious reactions, like trouble breathing and low blood pressure, can occur. You can be given medicine to prevent and treat allergic reactions, so be sure to tell your doctor if you have ever had a reaction to contrast material used for x-rays. It is also important to let your doctor know about any other allergies.

CT scans take longer than regular x-rays and you will need to lie still on a table while they are being done. But just like other computerized devices, they are getting faster and your stay might be pleasantly short. The newest CT scanners take only seconds to complete the study. Also, you might feel a bit confined by the ring-like equipment you're in when the pictures are being taken.

CT scans are sometimes used to guide a biopsy needle precisely into an area of suspected cancer spread. For this procedure, called a CT-guided needle biopsy, the patient remains on the CT scanning table while a radiologist advances a biopsy needle toward the location of the mass. CT scans are repeated until the doctors are confident that the needle is within the mass. A fine needle biopsy sample (tiny fragment of tissue) or a core needle biopsy sample (a thin cylinder of tissue about ½-inch long and less than 1/8-inch in diameter) is removed and examined under a microscope.

Magnetic resonance imaging (MRI): MRI scans use radio waves and strong magnets instead of x-rays to take pictures. The energy from the radio waves is absorbed and then released in a pattern formed by the type of tissue and by certain diseases. A computer translates the pattern of radio waves given off by the tissues into a very detailed image of parts of the body. Not only does this produce cross sectional slices of the body like a CT scanner, it can also produce slices that are parallel with the length of your body.

MRI images are particularly useful in examining pelvic tumors. They are also helpful in detecting cancer that has spread to the brain or spinal cord.

A contrast material might be injected just as with CT scans, but is used less often. MRI scans take longer than CTs -- often up to an hour. Also, you have to be placed inside a tube-like piece of equipment, which is confining and can upset people with claustrophobia (a fear of enclosed spaces). The machine makes a thumping noise that some people find disturbing. Some places provide headphones with music to block this noise out. A mild sedative is helpful for some people.

Intravenous urography: Intravenous urography (also known as intravenous pyelogram, or IVP) is an x-ray of the urinary system taken after a special dye is injected into a vein. This

dye is removed from the bloodstream by the kidneys and passes into the ureters and bladder (the ureters are the tubes that connect the kidneys to the bladder). This test finds abnormalities in the urinary tract, such as changes caused by spread of cervical cancer to the pelvic lymph nodes, which may compress or block a ureter. IVP is rarely used currently to evaluate patients with cervical cancer. You will not usually need an IVP if you have already had a CT or MRI.

Positron emission tomography: Positron emission tomography (PET) uses glucose (a form of sugar) that contains a radioactive atom. Cancer cells in the body absorb large amounts of the radioactive sugar and a special camera can detect the radioactivity. This test can help see if the cancer has spread to lymph nodes. PET scans are also useful when your doctor thinks the cancer has spread but doesn't know where. PET scans can be used instead of several different x-rays because they scan your whole body. Newer devices combine a CT scan and a PET scan to even better pinpoint the tumor. This test is rarely used for patients with early cervical cancer, but may be used to look for more advanced disease.

How is cervical cancer staged?

The process of finding out how far the cancer has spread is called staging. Information from exams and diagnostic tests is used to determine the size of the tumor, how deeply the tumor has invaded tissues within and around the cervix, and the spread to lymph nodes or distant organs (metastasis). This is an important process because the stage of the cancer is the key factor in selecting the right treatment plan.

A staging system is a way for members of the cancer care team to summarize the extent of a cancer's spread. The 2 systems used for staging most types of cervical cancer, the *FIGO* (International Federation of Gynecology and Obstetrics) system and the American Joint Committee on Cancer TNM staging system, are very similar. They both classify cervical cancer on the basis of 3 factors: the extent of the tumor (T), whether the cancer has spread to lymph nodes (N) and whether it has spread to distant sites (M). The system described below is the most recent AJCC system, which went into effect January 2010. Any differences between the AJCC system and the FIGO system are explained in the text.

This system classifies the disease in stages 0 through IV. It is based on clinical staging rather than surgical staging. This means that the extent of disease is evaluated by the doctor's physical examination and a few other tests that are done in some cases, such as cystoscopy and proctoscopy -- it is not based on the findings at surgery.

If surgery is done, it may show that the cancer has spread more than the doctors first thought. This new information may change the treatment plan, but it does not change the patient's stage.

Tumor extent (T)

Tis: The cancer cells are only found on the surface of the cervix (in the layer of cells lining the cervix), without growing into deeper tissues. (Tis is not included in the FIGO system)

T1: The cancer cells have grown from the surface layer of the cervix into deeper tissues of the cervix. The cancer may also be growing into the body of the uterus, but it has not grown outside of the uterus.

T1a: There is a very small amount of cancer, and it can be seen only under a microscope.

T1a1: The area of cancer is less than 3 mm (about 1/8-inch) deep and less than 7 mm (about 1/4-inch) wide.

T1a2: The area of cancer invasion is between 3 mm and 5 mm (about 1/5-inch) deep and less than 7 mm (about 1/4-inch) wide.

T1b: This stage includes stage I cancers that can be seen without a microscope. This stage also includes cancers that can only be seen with a microscope if they have spread deeper than 5 mm (about 1/5 inch) into connective tissue of the cervix or are wider than 7 mm.

T1b1: The cancer can be seen but it is not larger than 4 cm (about 1 3/5 inches).

T1b2: The cancer can be seen and is larger than 4 cm.

T2: In this stage, the cancer has grown beyond the cervix and uterus, but hasn't spread to the walls of the pelvis or the lower part of the vagina. The cancer may have grown into the upper part of the vagina.

T2a: The cancer has not spread into the tissues next to the cervix (called the parametria).

T2a1: The cancer can be seen but it is not larger than 4 cm (about 1 3/5 inches).

T2a2: The cancer can be seen and is larger than 4 cm.

T2b: The cancer has spread into the tissues next to the cervix (the parametria)

T3: The cancer has spread to the lower part of the vagina or the walls of the pelvis. The cancer may be blocking the ureters (tubes that carry urine from the kidneys to the bladder).

T3a: The cancer has spread to the lower third of the vagina but not to the walls of the pelvis.

T3b: The cancer has grown into the walls of the pelvis and/or is blocking one or both ureters (this is called hydronephrosis).

T4: The cancer has spread to the bladder or rectum or it is growing out of the pelvis

Lymph node spread (N)

NX: The nearby lymph nodes cannot be assessed

N0: No spread to nearby lymph nodes

N1: The cancer has spread to nearby lymph nodes

Distant spread (M)

M0: The cancer has not spread to distant lymph nodes, organs, or tissues

M1: The cancer has spread to distant organs (such as the lungs or liver), to lymph nodes in the chest or neck, and/or to the peritoneum (the tissue coating the inside of the abdomen).

Stage grouping

Information about the tumor, lymph nodes, and any cancer spread is then combined to assign the stage of disease. This process is called stage grouping. The stages are described using the number 0 and Roman numerals from I to IV. Some stages are divided into sub-stages indicated by letters and numbers.

Stage 0 (Tis, N0, M0): The cancer cells are only in the cells on the surface of the cervix (the layer of cells lining the cervix), without growing into (invading) deeper tissues of the cervix. This stage is also called carcinoma in situ (CIS) or cervical intraepithelial neoplasia (CIN) grade III (CIN III). This stage is not included in the FIGO system.

Stage I (T1, N0, M0): In this stage the cancer has grown into (invaded) the cervix, but it is not growing outside the uterus. The cancer has not spread to nearby lymph nodes (N0) or distant sites (M0).

Stage IA (T1a, N0, M0): This is the earliest form of stage I. There is a very small amount of cancer, and it can be seen only under a microscope. The cancer has not spread to nearby lymph nodes (N0) or distant sites (M0).

- **Stage IA1 (T1a1, N0, M0):** The cancer is less than 3 mm (about 1/8-inch) deep and less than 7 mm (about 1/4-inch) wide. The cancer has not spread to nearby lymph nodes (N0) or distant sites (M0).
- **Stage IA2 (T1a2, N0, M0):** The cancer is between 3 mm and 5 mm (about 1/5-inch) deep and less than 7 mm (about 1/4-inch) wide. The cancer has not spread to nearby lymph nodes (N0) or distant sites (M0).

Stage IB (T1b, N0, M0): This stage includes stage I cancers that can be seen without a microscope as well as cancers that can only be seen with a microscope if they have spread deeper than 5 mm (about 1/5 inch) into connective tissue of the cervix or are wider than 7 mm. These cancers have not spread to nearby lymph nodes (N0) or distant sites (M0).

- **Stage IB1 (T1b1, N0, M0):** The cancer can be seen but it is not larger than 4 cm (about 1 3/5 inches). It has not spread to nearby lymph nodes (N0) or distant sites (M0).
- **Stage IB2 (T1b2, N0, M0):** The cancer can be seen and is larger than 4 cm. It has not spread to nearby lymph nodes (N0) or distant sites (M0).

Stage II (T2, N0, M0): In this stage, the cancer has grown beyond the cervix and uterus, but hasn't spread to the walls of the pelvis or the lower part of the vagina.

Stage IIA (T2a, N0, M0): The cancer has not spread into the tissues next to the cervix (called the parametria). The cancer may have grown into the upper part of the vagina. It has not spread to nearby lymph nodes (N0) or distant sites (M0).

- **Stage IIA1 (T2a1, N0, M0):** The cancer can be seen but it is not larger than 4 cm (about 1 3/5 inches). It has not spread to nearby lymph nodes (N0) or distant sites (M0).
- **Stage IIA2 (T2a2, N0, M0):** The cancer can be seen and is larger than 4 cm. It has not spread to nearby lymph nodes (N0) or distant sites (M0).

Stage IIB (T2b, N0, M0): The cancer has spread into the tissues next to the cervix (the parametria). It has not spread to nearby lymph nodes (N0) or distant sites (M0).

Stage III (T3, N0, M0): The cancer has spread to the lower part of the vagina or the walls of the pelvis. The cancer may be blocking the ureters (tubes that carry urine from the kidneys to the bladder). It has not spread to nearby lymph nodes (N0) or distant sites (M0).

Stage IIIA (T3a, N0, M0): The cancer has spread to the lower third of the vagina but not to the walls of the pelvis. It has not spread to nearby lymph nodes (N0) or distant sites (M0).

Stage IIIB (T3b, N0, M0; OR T1-3, N1, M0): either:

- The cancer has grown into the walls of the pelvis and/or has blocked one or both ureters (a condition called hydronephrosis), but has not spread to lymph nodes or distant sites.

OR

- The cancer has spread to lymph nodes in the pelvis (N1) but not to distant sites (M0). The tumor can be any size and may have spread to the lower part of the vagina or walls of the pelvis (T1-T3).

Stage IV: This is the most advanced stage of cervical cancer. The cancer has spread to nearby organs or other parts of the body.

Stage IVA (T4, N0, M0): The cancer has spread to the bladder or rectum, which are organs close to the cervix (T4). It has not spread to nearby lymph nodes (N0) or distant sites (M0).

Stage IVB (any T, any N, M1): The cancer has spread to distant organs beyond the pelvic area, such as the lungs or liver.

Survival rates by stage

Survival rates are often used by doctors as a standard way of discussing a person's prognosis (outlook). Some patients with cancer may want to know the survival statistics for people in similar situations, while others may not find the numbers helpful, or may even not want to know them. Whether or not you want to read about the survival statistics below for cervical cancer is up to you.

The 5-year survival rate refers to the percentage of patients who live at least 5 years after their cancer is diagnosed. Of course, many people live much longer than 5 years (and many are cured).

In order to get 5-year survival rates, doctors have to look at people who were treated at least 5 years ago. Improvements in treatment since then may result in a more favorable outlook for people now being diagnosed with cervical cancer.

Survival rates are often based on previous outcomes of large numbers of people who had the disease, but they cannot predict what will happen in any particular person's case. Many other factors may affect a person's outlook, such as their general health and how well the cancer responds to treatment. Your doctor can tell you how the numbers below may apply to you, as he or she is familiar with the aspects of your particular situation.

The numbers below come from the National Cancer Data Base, and are based on people diagnosed between 2000 and 2002.

Stage	5-Year Survival Rate
0	93%
IA	93%
IB	80%
IIA	63%
IIB	58%
IIIA	35%

IIIB	32%
IVA	16%
IVB	15%

How is cervical cancer treated?

This information represents the views of the doctors and nurses serving on the American Cancer Society's Cancer Information Database Editorial Board. These views are based on their interpretation of studies published in medical journals, as well as their own professional experience.

The treatment information in this document is not official policy of the Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor.

Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

The options for treating each patient with cervical cancer depend on the stage of disease. The stage of a cancer describes its size, depth of invasion (how far it has grown into the cervix), and how far it has spread.

After establishing the stage of your cervical cancer, your cancer care team will recommend your treatment options. Think about your options without feeling rushed. If there is anything you do not understand, ask for an explanation. Although the choice of treatment depends largely on the stage of the disease at the time of diagnosis, other factors that may influence your options are your age, your general health, your individual circumstances, and your preferences. Be sure that you understand all the risks and side effects of the various treatments before making a decision.

It is often a good idea to get a second opinion, especially from doctors experienced in treating cervical cancer. A second opinion can give you more information and help you feel more confident about choosing a treatment plan. Some insurance companies require a second opinion before they will agree to pay for certain treatments. Almost all will pay for a second opinion. Still, you might want to check your coverage first, so you'll know if you will have to pay for it.

The 3 main methods of cancer treatment are surgery, radiation therapy, and chemotherapy. Sometimes the best treatment approach uses 2 or more of these methods. Your recovery is the goal of your cancer care team. If a cure is not possible, the goal may be to remove or destroy as much of the cancer as possible to help you live longer and feel better. Sometimes treatment is aimed at relieving symptoms. This is called *palliative treatment*.

Surgery

Cryosurgery

A metal probe cooled with liquid nitrogen is placed directly on the cervix. This kills the abnormal cells by freezing them. Cryosurgery is used to treat pre-invasive cervical cancer (stage 0), but not invasive cancer.

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. Laser surgery is used to treat pre-invasive cervical cancer (stage 0). It is not used to treat invasive cancer.

Conization

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). (See the section, "Can cervical cancer be prevented?" for more information.) A cone biopsy may be used to diagnose the cancer before additional treatment with surgery or radiation. It can also be used as the only treatment in women with early (stage IA1) cancer who want to preserve their ability to have children (fertility). After the biopsy, the tissue removed (the cone) is examined under the microscope. If the margins (outer edges) of the cone contain cancer (or pre-cancer) cells, further treatment will be needed to make sure that all of the cancer is removed.

Hysterectomy

This is surgery to remove the uterus (both the body of the uterus and the cervix) but not the structures next to the uterus (parametria and uterosacral ligaments). The vagina and pelvic lymph nodes are not removed. The ovaries and fallopian tubes are usually left in place unless there is some other reason to remove them.

When the uterus is removed through a surgical incision in the front of the abdomen, it is called an abdominal hysterectomy. When the uterus is removed through the vagina, it is called a *vaginal hysterectomy*. When the uterus is removed using laparoscopy, it is called a *laparoscopic hysterectomy*. In some cases, laparoscopy is performed with special tools to help the surgeon see better and with instruments that are controlled by the surgeon. This is called *robotic-assisted surgery*.

General or epidural (regional) anesthesia is used for all of these operations. The recovery time and hospital stay tends to be shorter for a laparoscopic or vaginal hysterectomy than for an abdominal hysterectomy. For a laparoscopic or vaginal hysterectomy, the hospital stay is usually 1 to 2 days followed by a 2- to 3-week recovery period. A hospital stay of 3 to 5 days is common for an abdominal hysterectomy, and complete recovery takes about 4 to 6 weeks. Any type of hysterectomy results in infertility (inability to have children). Complications are

unusual but could include excessive bleeding, wound infection, or damage to the urinary or intestinal systems.

Hysterectomy is used to treat stage IA1 cervical cancers. It is also used for some stage 0 cancers (carcinoma in situ), if cancer cells were found at the edges of the cone biopsy (this is called *positive margins*) or for adenocarcinoma in situ. A hysterectomy is also used to treat some non-cancerous conditions. The most common of these is leiomyomas, a type of benign tumor commonly known as fibroids.

Radical hysterectomy and pelvic lymph node dissection

For this operation the surgeon removes more than just the uterus. Also removed are the tissues next to the uterus (parametria and uterosacral ligaments), the upper part (about 1 inch) of the vagina next to the cervix, and some pelvic lymph nodes (pea-sized collections of immune system tissue). The ovaries and fallopian tubes are not removed unless there is some other medical reason to do so. This surgery is usually performed through an abdominal incision.

Another surgical approach is called laparoscopic-assisted radical vaginal hysterectomy. This operation combines a radical vaginal hysterectomy with a laparoscopic pelvic node dissection. Laparoscopy allows the inside of the abdomen and pelvis to be seen through a tube inserted into very small surgical incisions. Small instruments can be controlled through the tube, so the surgeon can remove lymph nodes through the tubes without making a large cut in the abdomen. The laparoscope can also make it easier for the doctor to remove the uterus, ovaries, and fallopian tubes through the vaginal incision.

Robot-assisted laparoscopic surgery is also sometimes used to perform radical hysterectomies. The advantages are lower blood loss and a shorter stay in the hospital after surgery. However, this way of treating cervical cancer is still relatively new, and its ultimate role in treatment is still being studied.

More tissue is removed in a radical hysterectomy than in a simple one, so the hospital stay can be longer, about 5 to 7 days. Because the uterus is removed, this surgery results in infertility. Complications are unusual but could include excessive bleeding, wound infection, or damage to the urinary and intestinal systems. A radical hysterectomy and pelvic lymph node dissection are the usual treatment for stages IA2, IB, and less commonly IIA cervical cancer, especially in young women.

Sexual impact of hysterectomy: Radical hysterectomy does not change a woman's ability to feel sexual pleasure. Although the vagina is shortened, the area around the clitoris and the lining of the vagina remains as sensitive as before. A woman does not need a uterus or cervix to reach orgasm. When cancer has caused pain or bleeding with intercourse, the hysterectomy may actually improve a woman's sex life by stopping these symptoms.

Trachelectomy

Most women with stage IA2 and stage IB are treated with hysterectomy. Another procedure, known as a radical trachelectomy, allows some of these young women to be treated without losing their ability to have children. This procedure removes the cervix and the upper part of the vagina and placing a "purse-string" stitch to act as an artificial internal opening of the cervix (the opening of the cervix inside the uterine cavity). The nearby lymph nodes are also removed using laparoscopy. The operation is done either through the vagina or the abdomen.

After trachelectomy, some women are able to carry a pregnancy to term and deliver a healthy baby by cesarean section. In one study, the pregnancy rate after 5 years was more than 50%, but the risk of miscarriage after this surgery was higher than what is seen in normal healthy women. The risk of the cancer coming back after this procedure is low.

Pelvic exenteration

This is a more extensive operation that may be used to treat recurrent cervical cancer. In this surgery, all of the organs and tissues are removed as in a radical hysterectomy with pelvic lymph node dissection. This operation may also remove the bladder, vagina, rectum, and part of the colon, depending on where the cancer has spread.

If the bladder is removed, a new way to store and eliminate urine will be needed. This usually means using a short segment of intestine to function as a new bladder. The new bladder may be connected to the abdominal wall so that urine is drained periodically when the patient places a catheter into a urostomy (a small opening). Or urine may drain continuously into a small plastic bag attached to the front of the abdomen.

If the rectum and part of the colon are removed, a new way to eliminate solid waste must be created. This is done by attaching the remaining intestine to the abdominal wall so that fecal material can pass through a colostomy (a small opening) into a small plastic bag worn on the front of the abdomen. It may be possible to remove the involved colon (next to the cervix) and reconnect the colon so that no bags or external appliances are needed. If the vagina is removed, a new vagina can be surgically created out of skin, intestinal tissue, or myocutaneous (muscle and skin) grafts.

Sexual impact of pelvic exenteration: Recovery from total pelvic exenteration takes a long time. Most women don't begin to feel like their normal selves again for 6 months after surgery. Some say it takes a year or two to adjust completely.

Nevertheless, these women can lead happy and productive lives. With practice and determination, they can also have sexual desire, pleasure, and orgasms.

Radiation therapy

Radiation therapy uses high energy x-rays to kill cancer cells. These x-rays may be given externally in a procedure that is much like having a diagnostic x-ray. This is called *external beam radiation therapy*. This treatment usually takes 6 to 7 weeks to complete. For cervical cancer, this type of radiation therapy is often given along with low doses of chemotherapy with a drug called *cisplatin*.

Another type of radiation therapy is called *brachytherapy*, or internal radiation therapy. For cervical cancer, the radioactive material is placed in a cylinder in the vagina. For some cancers, radioactive material may be placed in thin needles that are inserted directly in the tumor. Low-dose brachytherapy is completed in just a few days. During that time, the patient remains in the hospital with instruments holding the radioactive material in place. High-dose rate brachytherapy is done as an outpatient over several treatments. For each treatment, the radioactive material is inserted for a few minutes and then removed. The advantage of high-dose rate is that you do not have to stay still for long periods of time.

Common side effects of radiation therapy include tiredness, upset stomach, or loose bowels. Some people have problems with nausea and vomiting. These side effects tend to be worse when chemotherapy is given with radiation. Radiation can also lead to low blood counts, causing anemia (low red blood cells) and leukopenia (low white blood cells). The blood counts usually return to normal after radiation is stopped. Skin changes are also common, with the skin in the treated area looking and feeling sunburned. Pelvic radiation therapy may cause scar tissue to form in the vagina. The scar tissue can make the vagina more narrow (called *vaginal stenosis*) or even shorter, which makes sex (vaginal intercourse) painful. A woman can help prevent this problem by stretching the walls of her vagina several times a week. This can be done by engaging in sexual intercourse 3 to 4 times per week or by using a vaginal dilator (a plastic or rubber tube used to stretch out the vagina). Vaginal dryness and painful intercourse can be long-term side effects from radiation. Pelvic radiation can damage the ovaries, causing premature menopause. Radiation can irritate the bladder and problems with urination may occur. Vaginal (local) estrogens may also be used to help with vaginal dryness and atrophy. Radiation to the pelvis can also weaken the bones, leading to fractures. Hip fractures are the most common, and may occur 2 to 4 years after radiation. Bone density studies are recommended. Treating lymph nodes with radiation can lead to problems with drainage of fluid from the leg. This can cause severe swelling in the leg, a condition called *lymphedema*.

If you are having side effects from radiation, discuss them with your cancer care team.

It is important to know that smoking increases the side effects from radiation. If you smoke, you should stop.

Chemotherapy

Systemic chemotherapy uses anti-cancer drugs that are injected into a vein or given by mouth. These drugs enter the bloodstream and reach all areas of the body, making this treatment potentially useful for cancers that have spread to distant organs (metastasized).

Drugs most often used to treat cervical cancer include cisplatin, paclitaxel (Taxol®), topotecan, ifosfamide, and fluorouracil (5-FU). If chemotherapy is chosen, you may receive a combination of drugs. Chemotherapy drugs kill cancer cells but also damage some normal cells, which can lead to side effects.

Chemotherapy side effects depend on the type of drugs, the amount taken, and the length of time you are treated. Temporary side effects of chemotherapy might include:

- nausea and vomiting
- loss of appetite
- loss of hair
- mouth sores

Because chemotherapy can damage the blood-producing cells of the bone marrow, the blood cell counts might become low. This can result in:

- an increased chance of infection (from a shortage of white blood cells)
- bleeding or bruising after minor cuts or injuries (because of a shortage of blood platelets)
- shortness of breath (due to low red blood cell counts)

Fatigue is also quite common and may be caused by low red blood cell counts, by other reasons related to the chemotherapy, or by the cancer itself.

Most side effects of chemotherapy (except premature menopause and infertility) disappear once treatment is stopped. Hair will grow back after treatment ends. Premature menopause can be treated with hormones.

If you have problems with side effects, talk with your cancer care team. There are remedies for many of the temporary side effects of chemotherapy. For example, there are very good drugs that can prevent or reduce nausea and vomiting. Other drugs can be given to boost blood cell production.

For some stages of cervical cancer, chemotherapy is given to help the radiation work better. When chemotherapy and radiation therapy are given together, it is called *concurrent* chemoradiation. One option is to give a dose of cisplatin every week during radiation. This drug is given into a vein (IV) about 4 hours before the radiation appointment. Another choice is to give cisplatin along with fluorouracil (5-FU) every 4 weeks during radiation. Other drug combinations are also used. Giving chemotherapy with radiation can improve the patient's outlook, but giving the 2 together also tends to have worse side effects. The nausea and fatigue are often worse. Diarrhea can also be a problem if chemotherapy is given at the same

time as radiation. Problems with low blood counts can also be worse. Your health care team will watch for side effects and can give you medicines to help you feel better.

Clinical trials

You may have had to make a lot of decisions since you've been told you have cancer. One of the most important decisions you will make is choosing which treatment is best for you. You may have heard about clinical trials being done for your type of cancer. Or maybe someone on your health care team has mentioned a clinical trial to you.

Clinical trials are carefully controlled research studies that are done with patients who volunteer for them. They are done to get a closer look at promising new treatments or procedures.

If you would like to take part in a clinical trial, you should start by asking your doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service for a list of clinical trials that meet your medical needs. You can reach this service at 1-800-303-5691 or on our Web site at <http://clinicaltrials.cancer.org>. You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll-free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials Web site at www.cancer.gov/clinicaltrials.

There are requirements you must meet to take part in any clinical trial. If you do qualify for a clinical trial, it is up to you whether or not to enter (enroll in) it.

Clinical trials are one way to get state-of-the-art cancer treatment. They are the only way for doctors to learn better methods to treat cancer. Still, they are not right for everyone.

You can get a lot more information on clinical trials in our document called *Clinical Trials: What You Need to Know*. You can read it on our Web site or call our toll-free number (1-800-227-2345) and have it sent to you.

Complementary and alternative therapies

When you have cancer you are likely to hear about ways to treat your cancer or relieve symptoms that your doctor hasn't mentioned. Everyone from friends and family to Internet groups and Web sites offer ideas for what might help you. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

What exactly are complementary and alternative therapies?

Not everyone uses these terms the same way, and they are used to refer to many different methods, so it can be confusing. We use *complementary* to refer to treatments that are used *along with* your regular medical care. *Alternative* treatments are used *instead of* a doctor's medical treatment.

Complementary methods: Most complementary treatment methods are not offered as cures for cancer. Mainly, they are used to help you feel better. Some methods that are used along with regular treatment are meditation to reduce stress, acupuncture to help relieve pain, or peppermint tea to relieve nausea. Some complementary methods are known to help, while others have not been tested. Some have been proven not to be helpful, and a few have even been found harmful.

Alternative treatments: Alternative treatments may be offered as cancer cures. These treatments have not been proven safe and effective in clinical trials. Some of these methods may pose danger, or have life-threatening side effects. But the biggest danger in most cases is that you may lose the chance to be helped by standard medical treatment. Delays or interruptions in your medical treatments may give the cancer more time to grow and make it less likely that treatment will help.

Finding out more

It is easy to see why people with cancer think about alternative methods. You want to do all you can to fight the cancer, and the idea of a treatment with no side effects sounds great. Sometimes medical treatments like chemotherapy can be hard to take, or they may no longer be working. But the truth is that most of these alternative methods have not been tested and proven to work in treating cancer.

As you consider your options, here are 3 important steps you can take:

- Look for "red flags" that suggest fraud. Does the method promise to cure all or most cancers? Are you told not to have regular medical treatments? Is the treatment a "secret" that requires you to visit certain providers or travel to another country?
- Talk to your doctor or nurse about any method you are thinking about using
- Contact us at 1-800-ACS-2345 to learn more about complementary and alternative methods in general and to find out about the specific methods you are looking at.

The choice is yours

Decisions about how to treat or manage your cancer are always yours to make. If you want to use a non-standard treatment, learn all you can about the method and talk to your doctor about it. With good information and the support of your health care team, you may be able to safely use the methods that can help you while avoiding those that could be harmful.

Treatment options for cervical cancer by stage

The stage of a cervical cancer is the most important factor in choosing treatment. However, other factors that affect this decision include the exact location of the cancer within the cervix, the type of cancer (squamous cell or adenocarcinoma), your age, your overall physical condition, and whether you want to have children.

Stage 0 (carcinoma in situ)

Although the staging system classifies carcinoma in situ (CIS) as the earliest form of cancer, doctors often think of it as a pre-cancer. That is because the cancer cells in CIS are only in the surface layer of the cervix -- they have not grown into deeper layers of cells. Treatment options for squamous cell carcinoma in situ are the same as for other pre-cancers (dysplasia or cervical intraepithelial neoplasia [CIN]). Options include cryosurgery, laser surgery, loop electrosurgical excision procedure (LEEP/LEETZ), and cold knife conization. For adenocarcinoma in situ, hysterectomy is usually recommended. For those who wish to have children, treatment with a cone biopsy may be an option. No cancer cells must be found at the edges of the cone, and the patient must be closely watched as long as the cervix remains in place. After the woman has finished having children, a hysterectomy is recommended.

A simple hysterectomy is also an option for treatment of squamous cell carcinoma in situ, and may be done if it returns following other treatments. All cases of CIS can be cured with appropriate treatment. However, pre-cancerous changes can recur (come back) in the cervix or vagina, so it is very important for your doctor to watch you closely. This includes follow-up with regular Pap smears and in some instances with colposcopy.

Stage IA is divided into stage IA1 and stage IA2

Stage IA1: For this stage you have 3 options

- If you still want to be able to have children, first the cancer is removed with a cone biopsy, and then you are watched closely to see if the cancer comes back.
- If the cone biopsy doesn't remove all of the cancer (or if you are done having children), the uterus will be removed (hysterectomy).
- If the cancer has invaded the blood vessels or lymph vessels, you might need a radical hysterectomy along with removal of the pelvic lymph nodes.

Stage IA2: There are 3 treatment options

- radical hysterectomy along with removal of lymph nodes in the pelvis
- external beam radiation therapy plus brachytherapy

- radical trachelectomy with removal of pelvic lymph nodes can be done if you still wants to be able to have children

If you have surgery, the tissue removed will be examined in the laboratory to see if the cancer has spread further than expected. If the cancer has spread to the tissues next to the uterus (called the *parametria*) or to any lymph nodes, radiation therapy is usually recommended. Often chemotherapy will be given with the radiation therapy. If the pathology report says that the tumor had *positive margins*, this means that some cancer may have been left behind. This is also treated with pelvic radiation (given with cisplatin chemotherapy). The doctor may advise brachytherapy, as well.

Stage IB is divided into stage IB1 and stage IB2

Stage IB1: There are 3 options available:

- The standard treatment is a radical hysterectomy with removal of lymph nodes in the pelvis. Some lymph nodes from higher up in the abdomen (called *para-aortic lymph nodes*) are also removed to see if the cancer has spread there. If cancer cells are found in the edges of the tissues removed (positive margins) or if cancer cells are found in lymph nodes during this operation, radiation therapy may be given, possibly with chemotherapy, after surgery.
- The second treatment option is high-dose internal and external radiation therapy.
- Radical trachelectomy with removal of pelvic (and some para-aortic) lymph nodes is an option if the patient still wants to be able to have children

Stage IB2: There are 3 options available

- The standard treatment is the combination of chemotherapy with cisplatin and radiation therapy to the pelvis plus brachytherapy.
- Another choice is radical hysterectomy with removal of pelvic (and some para-aortic) lymph nodes. If cancer cells are found in the lymph nodes removed, or in the margins, radiation therapy may be given, possibly with chemotherapy, after surgery.
- Some doctors advise radiation given with chemotherapy (first option) followed by a hysterectomy.

Stage II is divided into stage IIA and stage IIB

Stage IIA: Treatment for this stage depends on the size of the tumor.

- One choice for treatment is brachytherapy and external radiation therapy. This is most often recommended if the tumor is larger than 4 cm (about 1½ inches). Chemotherapy with cisplatin will be given along with the radiation.
- Some experts recommend removing the uterus after the radiation therapy is done.
- If the cancer is not larger than 4 cm, it may be treated with a radical hysterectomy and removal of lymph nodes in the pelvis (and some in the para-aortic area). If the tissue removed at surgery shows cancer cells in the margins or cancer in the lymph nodes, radiation treatments to the pelvis will be given with chemotherapy. Brachytherapy may be given as well.

Stage IIB: Combined internal and external radiation therapy is the usual treatment. The radiation is given with the chemotherapy drug cisplatin. Sometimes other chemo drugs may be given along with cisplatin.

Stage III and IVA

Combined internal and external radiation therapy given with cisplatin is the recommended treatment.

If cancer has spread to the lymph nodes (especially those in the upper part of the abdomen) it can be a sign that the cancer has spread to other areas in the body. Some experts recommend checking the lymph nodes for cancer before giving radiation. One way to do this is by surgery. Another way is to do a CT or MRI scan to see how big the lymph nodes are. Lymph nodes that are bigger than usual are more likely to have cancer. Those lymph nodes can be biopsied to see if they contain cancer. If lymph nodes in the upper part of the abdomen (the para-aortic lymph nodes) are cancerous, doctors may want to do other tests to see if the cancer has spread to other parts of the body.

Stage IVB

At this stage, the cancer has spread out of the pelvis to other areas of the body. Stage IVB cervical cancer is not usually considered curable. Treatment options include radiation therapy to relieve the symptoms of cancer that has spread locally (near the cervix) or distant metastases. Chemotherapy is often recommended. Most standard regimens use a platinum compound (such as cisplatin or carboplatin) along with another drug such as paclitaxel, gemcitabine, topotecan, or vinorelbine. Clinical trials are testing other combinations of chemotherapy drugs, as well as some other experimental treatments.

Recurrent cervical cancer

Cancer that comes back after treatment is called *recurrent cancer*. Cancer can come back locally (in the pelvic organs near the cervix) or come back in distant areas (spread through the lymphatic system and/or the bloodstream to organs such as the lungs or bone).

If the cancer has recurred in the pelvis only, extensive surgery (by pelvic exenteration) may be an option for some patients. This operation may successfully treat 40% to 50% of patients. (See the discussion under Surgery in the section, "How is cervical cancer treated?") Sometimes radiation or chemotherapy may be used for palliative treatment (treatment to relieve symptoms but not expected to cure).

If your cancer has recurred in a distant area, chemotherapy or radiation therapy may be used to treat and relieve specific symptoms. If chemotherapy is used, you should understand the goals and limitations of this therapy. Sometimes chemotherapy can improve your quality of life, and other times it can diminish it. You need to discuss this with your doctors. Fifteen percent to 25% of patients may respond at least temporarily to chemotherapy.

New treatments that may benefit patients with distant recurrence of cervical cancer are being evaluated in clinical trials. You may want to think about participating in a clinical trial.

Cervical cancer in pregnancy

A small number of cervical cancers are found in pregnant women. If your cancer is a very early cancer, such as stage IA, then most doctors believe that it is safe to continue the pregnancy to term. Several weeks after delivery, a hysterectomy or a cone biopsy is recommended (the cone biopsy is suggested only for substage IA1).

If the cancer is stage IB, then you and your doctor must decide whether to continue the pregnancy. If not, treatment would be radical hysterectomy and/or radiation. If you decide to continue the pregnancy, the baby should be delivered by cesarean section as soon as it is able to survive outside the womb. More advanced cancers, should be treated immediately.

Financial help

In 2000, the Breast and Cervical Cancer Treatment Act was signed into law. This act provides funds to treat breast and cervical cancer for some low-income women. States must adopt the program in order to receive matching federal funds. For more information, you can contact the CDC at 1-888-842-6355 or on the Internet at www.cdc.gov/cancer.

More treatment information

For more details on treatment options -- including some that may not be addressed in this document -- the National Comprehensive Cancer Network (NCCN) and the National Cancer Institute (NCI) are good sources of information.

The NCCN, made up of experts from many of the nation's leading cancer centers, develops cancer treatment guidelines for doctors to use when treating patients. Those are available on the NCCN Web site (www.nccn.org).

The NCI provides treatment information via telephone (1-800-4-CANCER) and its Web site (www.cancer.gov). Information for patients as well as more detailed information intended for use by cancer care professionals is also available on www.cancer.gov.

What should you ask your doctor about cervical cancer?

It is important for you to have frank, open discussions with your cancer care team. They want to answer all of your questions, no matter how trivial you might think they are. Here are some questions to consider:

- What type of cervical cancer do I have?
- Has my cancer spread beyond the cervix?
- Can the stage of my cancer be determined and what does that mean?
- What are my treatment choices?
- What treatment do you recommend and why?
- What risks or side effects are there to the treatment you suggest?
- Will I be able to have children after my treatment?
- What are my treatment options if I want to have children in the future?
- What should I do to be ready for treatment?
- What are the chances my cancer will recur (come back) with the treatment programs we have discussed?
- Should I follow a special diet?
- Based on what you've learned about my cancer, what is my prognosis (outlook for chances of survival)?
- Where can I get a wig if I will receive chemotherapy drugs likely to cause temporary hair loss?
- What do I tell my children, husband, parents, and other family members?

In addition to these sample questions, be sure to write down some of your own. For instance, you might want specific information about anticipated recovery times so that you can plan your work schedule. Or you may want to ask about second opinions or about clinical trials for which you may qualify.

What happens after treatment for cervical cancer?

Completing treatment can be both stressful and exciting. You will be relieved to finish treatment, yet it is hard not to worry about cancer coming back. (When cancer returns, it is called recurrence.) This is a very common concern among those who have had cancer.

It may take a while before your confidence in your own recovery begins to feel real and your fears are somewhat relieved. Even with no recurrences, people who have had cancer learn to live with uncertainty.

Follow-up care

After your treatment is over, it is very important to keep all follow-up appointments. During these visits, your doctors will ask about symptoms, do physical exams, and order blood tests or imaging studies such as CT scans or x-rays. You will need to keep getting Pap tests no matter how you were treated (e.g., cone biopsy, hysterectomy, or radiation). Follow-up is needed to check for cancer recurrence or spread, as well as possible side effects of certain treatments. This is the time for you to ask your health care team any questions you need answered and to discuss any concerns you might have.

Almost any cancer treatment can have side effects. Some may last for a few weeks to several months, but others can be permanent. Don't hesitate to tell your cancer care team about any symptoms or side effects that bother you so they can help you manage them.

It is also important to keep medical insurance. Even though no one wants to think of their cancer coming back, it is always a possibility. If it happens, the last thing you want is to have to worry about paying for treatment.

Seeing a new doctor

At some point after your cancer diagnosis and treatment, you may find yourself in the office of a new doctor. Your original doctor may have moved or retired, or you may have moved or changed doctors for some reason. It is important that you be able to give your new doctor the exact details of your diagnosis and treatment. Make sure you have the following information handy:

- a copy of your pathology report from any biopsy or surgery
- if you had surgery, a copy of your operative report
- if you had radiation, a copy of the treatment summary
- if you were hospitalized, a copy of the discharge summary that every doctor must prepare when patients are sent home from the hospital

- finally, since some drugs can have long-term side effects, a list of your drugs (especially any chemotherapy drugs), drug doses, and when you took them

Lifestyle changes to consider during and after treatment

Having cancer and dealing with treatment can be time-consuming and emotionally draining, but it can also be a time to look at your life in new ways. Maybe you are thinking about how to improve your health over the long term. Some people even begin this process during cancer treatment.

Make healthier choices

Think about your life before you learned you had cancer. Were there things you did that might have made you less healthy? Maybe you drank too much alcohol, or ate more than you needed, or smoked, or didn't exercise very often. Emotionally, maybe you kept your feelings bottled up, or maybe you let stressful situations go on too long.

Now is not the time to feel guilty or to blame yourself. However, you can start making changes today that can have positive effects for the rest of your life. Not only will you feel better but you will also be healthier. What better time than now to take advantage of the motivation you have as a result of going through a life-changing experience like having cancer?

You can start by working on those things that you feel most concerned about. Get help with those that are harder for you. For instance, if you are thinking about quitting smoking and need help, call the American Cancer Society's Quitline® tobacco cessation program at 1-800-227-2345.

Diet and nutrition

Eating right can be a challenge for anyone, but it can get even tougher during and after cancer treatment. For instance, treatment often may change your sense of taste. Nausea can be a problem. You may lose your appetite for a while and lose weight when you don't want to. On the other hand, some people gain weight even without eating more. This can be frustrating, too.

If you are losing weight or have taste problems during treatment, do the best you can with eating and remember that these problems usually improve over time. You may want to ask your cancer team for a referral to a dietitian, an expert in nutrition who can give you ideas on how to fight some of the side effects of your treatment. You may also find it helps to eat small portions every 2 to 3 hours until you feel better and can go back to a more normal schedule.

One of the best things you can do after treatment is to start healthy eating habits. You will be surprised at the long-term benefits of some simple changes, like increasing the variety of healthy foods you eat. Try to eat 5 or more servings of vegetables and fruits each day. Choose whole grain foods instead of white flour and sugars. Try to limit meats that are high in fat. Cut back on processed meats like hot dogs, bologna, and bacon. Get rid of them altogether if you can. If you drink alcohol, limit yourself to 1 or 2 drinks a day at the most. And don't forget to get some type of regular exercise. The combination of a good diet and regular exercise will help you maintain a healthy weight and keep you feeling more energetic.

Rest, fatigue, work, and exercise

Fatigue is a very common symptom in people being treated for cancer. This is often not an ordinary type of tiredness but a bone-weary exhaustion that doesn't get better with rest. For some, this fatigue lasts a long time after treatment, and can discourage them from physical activity.

However, exercise can actually help you reduce fatigue. Studies have shown that patients who follow an exercise program tailored to their personal needs feel physically and emotionally improved and can cope better.

If you are ill and need to be on bed rest during treatment, it is normal to expect your fitness, endurance, and muscle strength to decline some. Physical therapy can help you maintain strength and range of motion in your muscles, which can help fight fatigue and the sense of depression that sometimes comes with feeling so tired.

Any physical activity program should fit your own situation. An older person who has never exercised will not be able to take on the same amount of exercise as a 20-year-old who plays tennis 3 times a week. If you haven't exercised in a few years but can still get around, you may want to think about taking short walks.

Talk with your health care team before starting, and get their opinion about your exercise plans. Then, try to get an exercise buddy so that you're not doing it alone. Having family or friends involved when starting a new exercise program can give you that extra boost of support to keep you going when the push just isn't there.

If you are very tired, though, you will need to balance activity with rest. It is okay to rest when you need to. It is really hard for some people to allow themselves to do that when they are used to working all day or taking care of a household. (For more information about fatigue, please see the publication, *Fatigue in People with Cancer*.)

Exercise can improve your physical and emotional health.

- It improves your cardiovascular (heart and circulation) fitness.
- It strengthens your muscles.
- It reduces fatigue.
- It lowers anxiety and depression.
- It makes you feel generally happier.
- It helps you feel better about yourself.

And over a lifetime, we know that exercise plays a role in preventing some cancers. The American Cancer Society, in its guidelines on physical activity for cancer prevention, recommends that adults take part in at least 1 physical activity for 30 minutes or more on 5 days or more of the week. Children and teens are encouraged to try for at least 60 minutes a day of energetic physical activity on at least 5 days a week.

How about your emotional health?

Once your treatment ends, you may find yourself overwhelmed by emotions. This happens to a lot of people. You may have been going through so much during treatment that you could only focus on getting through your treatment.

Now you may find that you think about the potential of your own death, or the effect of your cancer on your family, friends, and career. You may also begin to re-evaluate your relationship with your spouse or partner. Unexpected issues may also cause concern -- for instance, as you become healthier and have fewer doctor visits, you will see your health care team less often. That can be a source of anxiety for some.

This is an ideal time to seek out emotional and social support. You need people you can turn to for strength and comfort. Support can come in many forms: family, friends, cancer support groups, church or spiritual groups, online support communities, or individual counselors.

Almost everyone who has been through cancer can benefit from getting some type of support. What's best for you depends on your situation and personality. Some people feel safe in peer-support groups or education groups. Others would rather talk in an informal setting, such as church. Others may feel more at ease talking one-on-one with a trusted friend or counselor. Whatever your source of strength or comfort, make sure you have a place to go with your concerns.

The cancer journey can feel very lonely. It is not necessary or realistic to go it all by yourself. And your friends and family may feel shut out if you decide not to include them. Let them in -- and let in anyone else who you feel may help. If you aren't sure who can help, call your American Cancer Society at 1-800-227-2345 and we can put you in touch with an appropriate group or resource.

You can't change the fact that you have had cancer. What you can change is how you live the rest of your life -- making healthy choices and feeling as well as possible, physically and emotionally.

What happens if treatment is no longer working?

If cancer continues to grow after one kind of treatment, or if it returns, it is often possible to try another treatment plan that might still cure the cancer, or at least shrink the tumors enough to help you live longer and feel better. On the other hand, when a person has received several different medical treatments and the cancer has not been cured, over time the cancer tends to become resistant to all treatment. At this time it's important to weigh the possible limited benefit of a new treatment against the possible downsides, including continued doctor visits and treatment side effects.

Everyone has his or her own way of looking at this. Some people may want to focus on remaining comfortable during their limited time left.

This is likely to be the most difficult time in your battle with cancer -- when you have tried everything medically within reason and it's just not working anymore. Although your doctor may offer you new treatment, you need to consider that at some point, continuing treatment is not likely to improve your health or change your prognosis or survival.

If you want to continue treatment to fight your cancer as long as you can, you still need to consider the odds of more treatment having any benefit. In many cases, your doctor can estimate the response rate for the treatment you are considering. Some people are tempted to try more chemotherapy or radiation, for example, even when their doctors say that the odds of benefit are less than 1%. In this situation, you need to think about and understand your reasons for choosing this plan.

No matter what you decide to do, it is important that you be as comfortable as possible. Make sure you are asking for and getting treatment for any symptoms you might have, such as pain. This type of treatment is called "palliative" treatment.

Palliative treatment helps relieve these symptoms, but is not expected to cure the disease; its main purpose is to improve your quality of life. Sometimes, the treatments you get to control your symptoms are similar to the treatments used to treat cancer. For example, radiation therapy might be given to help relieve bone pain from bone metastasis. Or chemotherapy might be given to help shrink a tumor and keep it from causing a bowel obstruction. But this is not the same as receiving treatment to try to cure the cancer.

At some point, you may benefit from hospice care. Most of the time, this is given at home. Your cancer may cause symptoms or problems that need attention, and hospice focuses on your comfort. You should know that receiving hospice care doesn't mean you can't have treatment for the problems caused by your cancer or other health conditions. It just means

that the focus of your care is on living life as fully as possible and feeling as well as you can at this difficult stage of your cancer.

Remember also that maintaining hope is important. Your hope for a cure may not be as bright, but there is still hope for good times with family and friends -- times that are filled with happiness and meaning. In a way, pausing at this time in your cancer treatment is an opportunity to refocus on the most important things in your life. This is the time to do some things you've always wanted to do and to stop doing the things you no longer want to do.

What's new in cervical cancer research and treatment?

New ways to prevent and treat cancer of the cervix are being researched. Some of the promising new developments include the following:

HPV vaccines

Vaccines have been developed to prevent infection with some of the HPV types associated with cervical cancer. Currently available vaccines are intended to produce immunity to HPV types 16 and 18, so that women who are exposed to these viruses will not develop infections. Vaccines are also being developed to prevent infection with some of the other HPV types that also cause cancer. Long-term studies are being done to see how well these vaccines will reduce the risk of cervical cancer.

Some experimental vaccines are also being studied for women with established HPV infections, to help their immune systems destroy the virus and cure the infection before a cancer develops. Still other vaccines are meant to help women who already have advanced cervical cancer that has recurred or metastasized. These vaccines attempt to produce an immune reaction to the parts of the virus (E6 and E7 proteins) that make the cervical cancer cells grow abnormally. It is hoped that this immunity will kill the cancer cells or stop them from growing.

Other clinical trials

Many clinical trials are under way to test new chemotherapy drugs, new ways of giving radiation therapy, and new combinations of surgery and radiation therapy or chemotherapy.

Additional resources

More information from your American Cancer Society

We have selected some related information that may also be helpful to you. These materials may be ordered from our toll-free number, 1-800-227-2345.

After Diagnosis: a Guide for Patients and Families (also available in Spanish)

Home Care for the Person with Cancer: a Guide for Patients and Families (also available in Spanish)

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

Understanding Chemotherapy: a Guide for Patients and Families (also available in Spanish)

Understanding Radiation Therapy: a Guide for Patients and Families (also available in Spanish)

Sexuality for the Woman with Cancer (also available in Spanish)

The following books are available from the American Cancer Society. Call us at 1-800-ACS-2345 to ask about costs or to place your order.

Cancer in the Family: Helping Children Cope with a Parent's Illness

Caregiving: A Step-By-Step Resource for Caring for the Person with Cancer at Home

Crossing Divides: a Couple's Story of Cancer, Hope, and Hiking in the Montana Continental Divide

What Helped Get Me Through: Cancer Patients Share Wisdom and Hope

National organizations and Web sites*

In addition to the American Cancer Society, other sources of patient information and support include:

Gynecologic Cancer Foundation

Toll-free number: 1-800-444-4441

Telephone number: 1-312-578-1439

Web site: www.thegcf.org

National Cancer Institute

Toll-free number: 1-800-4-CANCER (1-800-422-6237)

Web site: www.cancer.gov

National Cervical Cancer Coalition

Toll-free number: 1-800- 685-5531

Telephone number: 1-818-909-3849

Web site: www.nccc-online.org

National Coalition for Cancer Survivorship

Toll-free number: 1-877-NCCS-YES (1-877-622-7937)

Web site: www.canceradvocacy.org

Centers for Disease Control and Prevention (CDC)

DES Update

Toll-free number: 1-888-232-6789

Web site: www.cdc.gov/des

**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.

References

Adam E, Kaufman RH, Adler-Storthz K, Melnick JL, Dreesman GR. A prospective study of association of herpes simplex virus and human papillomavirus infection with cervical neoplasia in women exposed to diethylstilbestrol in utero. *Int J Cancer*. 1985 Jan 15;35(1):19–26.

Advisory Committee on Immunization Practices. ACIP provisional recommendations for HPV vaccine. Available at: <http://www.cdc.gov/vaccines/recs/provisional/downloads/hpv-vac-dec2009-508.pdf>. Accessed 1/13/2010.

American Cancer Society. *Cancer Facts and Figures 2009*. Atlanta, Ga: American Cancer Society; 2009.

American Joint Committee on Cancer. Cervix Uteri. In: *AJCC Cancer Staging Manual*. 7th ed. New York, NY: Springer; 2010: 395-402.

Ault KA, Future II study group. Effect of prophylactic human papillomavirus L1 virus-like-particle vaccine on risk of cervical intraepithelial neoplasia grade 2, grade 3, and adenocarcinoma in situ: a combined analysis of four randomised clinical trials. *Lancet*. 2007 Jun 2;369(9576):1861–1868.

Eifel PJ, Berek JS, Markman, M. Cancer of the cervix, vagina, and vulva. In: DeVita VT, Hellman S, Rosenberg SA, eds. *Cancer: Principles and Practice of Oncology* 8th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2008: 1496–1543.

Ghosh C, Baker JA, Moysich KB, Rivera R, Brasure JR, McCann SE. Dietary intakes of selected nutrients and food groups and risk of cervical cancer. *Nutr Cancer*. 2008;60(3):331–341.

Hatch EE, Herbst AL, Hoover RN, Noller KL, Adam E, Kaufman RH, Palmer JR, Titus-Ernstoff L, Hyer M, Hartge P, Robboy SJ. Incidence of squamous neoplasia of the cervix and vagina in women exposed prenatally to diethylstilbestrol (United States). *Cancer Causes Control*. 2001 Nov;12(9):837–845.

International Collaboration of Epidemiological Studies of Cervical Cancer. Cervical cancer and reproductive factors: Collaborative reanalysis of individual data on 16,563 women with cervical carcinoma and 33,542 women without cervical carcinoma from 25 epidemiological studies. *Int J Cancer*. 2006;119:1108–1124.

International Collaboration of Epidemiological Studies of Cervical Cancer. Appleby P, Beral V, Berrington de González A, Colin D, Franceschi S, Goodhill A, Green J, Peto J, Plummer M, Sweetland S. Cervical cancer and hormonal contraceptives: collaborative reanalysis of individual data for 16,573 women with cervical cancer and 35,509 women without cervical cancer from 24 epidemiological studies. *Lancet*. 2007 Nov 10;370(9599):1609–1621.

Jhingran A, Eifel PJ, Wharton JT, et al. Neoplasms of the cervix. In: Kufe DW, Pollock RE, Weichselbaum RR, Bast RC, Gansler TS, Holland JF, Frei E. *Cancer Medicine* 6. Hamilton, Ontario: BC Decker; 2003. 1779–1808.

Jhingran A, Russel AH, Seiden MV, Duska LR, et al. Cancers of the cervix, vagina and vulva. In: Abeloff MD, Armitage JO, Lichter AS, et al. *Clinical Oncology*. 4th ed. Philadelphia, Pa; Elsevier; 2008: 1745–1765.

Kosary CL. Cancer of the uterine cervix. In: Ries LAG, Young JL, Keel GE, Eisner MP, Lin YD, Horner M-J (editors). *SEER Survival Monograph: Cancer Survival Among Adults: U.S. SEER Program, 1988-2001, Patient and Tumor Characteristics*. National Cancer Institute, SEER Program, NIH Pub. No. 07-6215, Bethesda, MD, 2007.

Lacey JV Jr, Swanson CA, Brinton LA, Altekruse SF, Barnes WA, Gravitt PE, Greenberg MD, Hadjimichael OC, McGowan L, Mortel R, Schwartz PE, Kurman RJ, Hildesheim A. Obesity as a potential risk factor for adenocarcinomas and squamous cell carcinomas of the uterine cervix. *Cancer*. 2003 Aug 15;98(4):814–821.

Markowitz LE, Dunne EF, Saraiya M, Lawson HW, Chesson H, Unger ER; Centers for Disease Control and Prevention (CDC); Advisory Committee on Immunization Practices (ACIP). Quadrivalent Human Papillomavirus Vaccine: Recommendations of the Advisory

Committee on Immunization Practices (ACIP). MMWR Recomm Rep. 2007 Mar 23;56(RR-2):1-24.

NCCN Practice Guidelines in Oncology. Cervical Cancer Version 1.2009. Available at: www.nccn.org. Accessed June 2009.

Paavonen J, Naud P, Salmerón J, Wheeler CM, Chow SN, Apter D, Kitchener H, Castellsague X, Teixeira JC, Skinner SR, Hedrick J, Jaisamrarn U, Limson G, Garland S, Szarewski A, Romanowski B, Aoki FY, Schwarz TF, Poppe WA, Bosch FX, Jenkins D, Hardt K, Zahaf T, Descamps D, Struyf F, Lehtinen M, Dubin G; HPV PATRICIA Study Group, Greenacre M. Efficacy of human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine against cervical infection and precancer caused by oncogenic HPV types (PATRICIA): final analysis of a double-blind, randomised study in young women. *Lancet*. 2009 Jul 25;374(9686):301-14.

PDQ database. Cervical cancer. Bethesda, Md: National Cancer Institute; 2008. Available at: www.cancer.gov/ Accessed July 2009.

Ries LAG, Melbert D, Krapcho M, Mariotto A, Miller BA, Feuer EJ, Clegg L, Horner MJ, Howlader N, Eisner MP, Reichman M, Edwards BK (eds). SEER Cancer Statistics Review, 1975-2004, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2006/, based on November 2008 SEER data submission, posted to the SEER web site, 2009.

Ronco G, Cuzick J, Pierotti P, et al. Accuracy of liquid based versus conventional cytology: overall results of new technologies for cervical cancer screening: randomised controlled trial. *BMJ*. 2007 Jul 7;335(7609):28. Epub 2007 May 21.

Rose PG, Ali S, Watkins E, Thigpen JT, Deppe G, Clarke-Pearson DL, Insalaco S; Gynecologic Oncology Group. Long-term follow-up of a randomized trial comparing concurrent single agent cisplatin, cisplatin-based combination chemotherapy, or hydroxyurea during pelvic irradiation for locally advanced cervical cancer: a Gynecologic Oncology Group Study. *J Clin Oncol*. 2007 Jul 1;25(19):2804–2810.

Saslow D, Castle PE, Cox JT, et al. American Cancer Society guideline for human papillomavirus (HPV) vaccine use to prevent cervical cancer and its precursors. *CA Cancer J Clin*. 2007;57:7–28.

Schiffman M, Castle PE, Jeronimo J, Rodriguez AC, Wacholder S. Human papillomavirus and cervical cancer. *Lancet*. 2007 Sep 8;370(9590):890–907.

Schover LR. *Sexuality and Fertility After Cancer*. New York: Wiley; 1997.

Shepherd JH, Spencer C, Herod J, Ind TEJ. Radical vaginal trachelectomy as a fertility-sparing procedure in women with early-stage cervical cancer-cumulative pregnancy rate in a series of 123 women. *BJOG*. 2006;113:719–723.

Tokudome S, Suzuki S, Ichikawa H, Hosono A, Maeda K, Marumoto M, Arakawa K, Agawa H, Ghadimi R. Condom use promotes regression of cervical intraepithelial neoplasia and clearance of human papillomavirus: a randomized clinical trial. *Int J Cancer*. 2004 Oct 20;112(1):

Troisi R, Hatch EE, Titus-Ernstoff L, Hyer M, Palmer JR, Robboy SJ, Strohsnitter WC, Kaufman R, Herbst AL, Hoover RN. Cancer risk in women prenatally exposed to diethylstilbestrol. *Int J Cancer*. 2007 Jul 15;121(2):356–360.

Waggoner SE. Cervical cancer. *Lancet*. 2003;361:2217–2225.

Wright TC Jr, Massad LS, Dunton CJ, Spitzer M, Wilkinson EJ, Solomon D; 2006 American Society for Colposcopy and Cervical Pathology-sponsored Consensus Conference. 2006 consensus guidelines for the management of women with abnormal cervical cancer screening tests. *Am J Obstet Gynecol*. 2007 Oct;197(4):346–355.

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